"I would have everie man write what he knowes and no more."—MONTAIGNE

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EDITORIAL

THIOPENTONE (?) IN OBSTETRICS

WHO shall decide when doctors disagree? The answer in the case before us would seem to be our readers. In our March number Dr. Collier tells us, as the result of his experience with 100 cases of Caesarean section that "The hazards of general anaesthesia for Caesarean section can be reduced by avoiding the use of barbiturates and the prolonged administration of depressant anaesthetic agents, and by utilizing controlled respiration with a cuffed endotracheal tube." In the present number Dr. Crawford, from an experience of 250 obstetric cases, some normal, some requiring the use of forceps and some Caesarean sections, comes to quite a different conclusion. He admits that the thiopentone he uses (250 mg) passes the placental barrier but that "There was no clinical evidence in any case studied of foetal depression attributable to the anaesthesia." He believes also "That using thiopentone, difficulties of induction are minimal and that maternal and foetal oxygenation is maintained throughout anaesthesia." There are other methods of easing the burden of labour. Our predecessors used chloroform for nearly 100 years with conspicuous success; indeed it was thought that chloroform, however dangerous it might be in other conditions, was almost entirely free from danger when given to a woman in labour.

K. M. Heard, from an experience of 360 cases of Caesarean section, 51.4 per cent of which were done under spinal anaesthesia, says "Thus in the entire series of 360 babies spinal anaesthesia emerged with unquestionably the best record." The results as regards the mothers were at least as good as those by any other method. All this looks as if the man is more important than the method. It is essential that they should match. Dr. Babcock's famous dictum, "After a death under spinal anaesthesia the anaesthetist may often properly write his own name in the space on the certificate reserved for the cause of death," should be remembered, and also that this statement does not only apply to deaths under spinal anaesthesia. The method, the man, and the circumstances, have all to be taken into consideration to get the best results. Complicated methods suitable for well furnished hospitals must necessarily give way to simpler ways when the circumstances are less propitious.

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SOME ASPECTS OF OBSTETRIC ANAESTHESIA

BY

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INTRODUCTION

OF all the cases with which the anaesthetist is confronted, the obstetric patients present, as a group, the greatest problem and challenge. In this country, at least, there is a satisfactory agreement on the principles of dealing with most emergency and poor risk cases. In the cases of forceps delivery and Caesarean section, however, there is much confused thought, little agreement or method, and relatively little evidence of sound investigation.

In over 250 obstetrical cases personally anaesthetized by the method described below, there have been only four infant deaths. The first was a macerated stillbirth in the case of a patient suffering from severe eclampsia with repeated fits, who herself died shortly afterwards. The second was found at postmortem to have a tentorial tear with considerable intracranial haemorrhage. The third was found to have only a few petechial haemorrhages in the brain substance, but as there had been a considerably prolonged and strong forceps traction with numerous re-applications, it was felt that death could not be attributed to the anaesthesia. The fourth was one of twins delivered by Caesarean section for foetal distress. A second foetal heart had not been heard for some hours and there was gross meconium staining. On delivery the infant had obviously been dead for some hours and its lungs were flooded with meconium stained liquor. The case of eclampsia referred to above was the only maternal death.

PART I: THE USE OF THIOPENTONE SODIUM

In collaboration with P. O. KANE†

THE use of thiopentone in obstetric anaesthesia is viewed with distrust by many obstetricians and anaesthetists, and, in the textbooks, discussions of its use reveal conflicting viewpoints. Thus, in the case of Caesarean section, whilst Hewer (1953) and Evans (1954) are not opposed to its use, Lee (1950) prefers not to use it and Wylie (1953) recommends its use with much reserve. Its use is not mentioned either by Minnitt and Gillies (1948) or by Macintosh and Bannister (1952), the two standard textbooks on anaesthesia. Le Breque (1938) appears to have first described the use of thiopentone and hexobarbitone in obstetric anaesthesia, presenting data on 80 cases of normal and forceps delivery. Rucker (1943) used thiopentone in 100 cases in which perineal

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block or local abdominal wall block formed part of the technique. Neither of these two authors found any evidence of foetal death attributable to the anaesthesia. Hellmann et al. (1944) gave an account of 1,415 deliveries (including spontaneous, forceps and Caesarean section) in which up to 2 g thiopentone was administered. The foetal mortality in cases where the foetus was known to be alive before commencement of anaesthesia was 2.4 per cent. They measured maternal and foetal thiopentone blood levels in seven cases (in which the dosage varied from 350 mg to 1 g). It was not stated whether the drug was administered as single or multiple injections. From these seven results they concluded that there was a delay of about 12 minutes before the foetal thiopentone level became equal to the maternal level and they claimed that if delivery were delayed beyond this time, foetal blood concentration of thiopentone might reach a dangerously high level. This "12-minute rule" has been repeated with modifications throughout the subsequent literature (Mazzola, 1947; Cooley and Schwarz, 1948; Herrick, 1948; Boyd and Jones, 1950; Mazzola, et al., 1952; Adriani, 1952; Flowers, 1953; Hershenson, 1954; and Wylie, 1953). None of these authors has published any data on blood levels of thiopentone. On the other hand, Cohen et al. (1953), who reported 124 cases, in 7 of which blood levels were measured, concluded that the time taken over delivery was of little consequence in relation to the degree of neonatal depression, and, indeed, that the longer the lapse of time, the less is the likelihood of the drug affecting the infant. Thomas and Gibson (1953) described cases in which the time from induction to delivery varied from 6 to 30 minutes "without demonstrable depression of the foetus."

In view of these conflicting reports, the work to be described below was undertaken.

(a) *Clinical Investigation.*

For forceps delivery, patients were placed in the lithotomy position and catheterized, the skin prepared and towels applied. Premedication consisted of atropine 1/100 grain (0.7 mg) only. Thiopentone (approx. 250 mg), given by intravenous injection taking less than one minute, invariably produced sleep. Anaesthesia was maintained with cyclopropane (200–600 ml/min) and oxygen (5–6 l./min). Obstetric manoeuvres were begun immediately the mask was applied. About 30 per cent of the patients showed reflex withdrawal on the commencement of surgery. These were quietened within a minute by increasing the cyclopropane flow rate. The cyclopropane was discontinued immediately the foetal head was crowned and a high flow of oxygen supplied until the umbilical cord had been clamped, after which further cyclopropane was administered until the episiotomy had been repaired.

In cases of Caesarean section, the procedure was identical except that anaesthesia was commenced before skin preparation, with the patient already on the operating table, and a relaxant drug was administered (see Part II).

Maternal blood samples were taken in 41 cases, 2 minutes after the conclusion of the thiopentone injection (A), at the time of clamping the cord (B), and a

sample of foetal blood was taken from the cord (C). Since samples of cord blood were taken from the placental end of the cord, there was often a delay of several minutes after clamping the cord before the samples could be obtained. If placental transmission persisted during this time, the results obtained would not represent actual neonatal levels. For this reason, the time at which placental transmission ceased was determined as described in the appendix, and was found to be concurrent with the time of completion of delivery.

The exact time between concluding the injection and clamping the cord was noted and that between clamping the cord and the first adequate cry of the infant. A record was kept of maternal and infant weights. In cases of Caesarean section, a sample of amniotic fluid was obtained, for analysis where possible.

In the hope of establishing a correlation between serum thiopentone level and depth of anaesthesia, a series of twelve volunteers (nonmaternity) were investigated as follows:

Samples of blood were taken 2 minutes after concluding an injection of approximately 250 mg thiopentone and again 3 or 5 minutes later. If the subject was still asleep a further sample was taken after 10 minutes. The time of awakening was noted.

(b) *Laboratory Investigation.*

Serum was separated from the blood samples and the thiopentone concentration estimated using the extraction procedure of Goldbaum (1948) combined with a slight variation of the ultraviolet absorption method of Gould and Hine (1949) using a Unicam SP500 spectrophotometer with 1-cm quartz cells. Results have been obtained and discarded on a further 18 cases using the continuous extraction procedure of Gould and Hine. Check experiments on serum containing known concentrations of thiopentone showed that recoveries by this procedure were erratic.

The ultraviolet spectrum usually consisted of a minimum of absorption at approximately 270 mμ and a maximum near 305 mμ and reached a constant low density above 350 mμ. In order to correct for the background absorption due to material extracted from the serum, a tangent was drawn between the minimum and the curve at about 350 mμ. The difference between the optical density at 305 mμ and the intercept of this tangent with the 305 mμ abscissa was proportional to the amount of thiopentone in the sample of serum (see figure 1). This method of blank correction was found to give more accurate results than that of Gould and Hine. We have confirmed Gould and Hine's observation that dif-

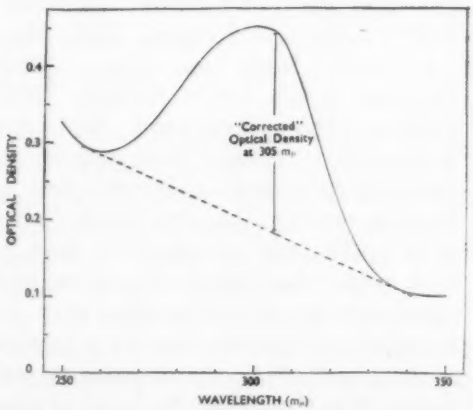

FIG. 1

Spectrum of thiopentone extracted from maternal serum.

ferent sera did not produce an equal "blank" correction as stated by Goldbaum (1948). Using this method a "corrected optical density" at 305 mμ of 1.00 was equivalent to 79.2 gamma of thiopentone sodium, and in the range 5–20 gamma thiopentone sodium in 1–2 ml of fluid, the results were reproducible to ±10 per cent for samples of human whole blood, serum and plasma and for rabbit serum to which known amounts of thiopentone had been added. Below 5 gamma thiopentone sodium the reproducibility of results was ±0.5 gamma.

The exact dosage was measured as follows: (i) Exactly 10 ml of water from a calibrated syringe was added to 500 mg thiopentone. (ii) About 5 ml was used for injection. (iii) The volume and thiopentone concentration of the remaining solution was measured.

All results were based on ultraviolet absorption measurements on a sample of thiopentone (free acid) which had been recrystallized from chloroform/light petroleum and whose purity was established by micro-analysis (found that C = 54.4%, H = 7.3%, N = 11.5%. Reqd. for $C_{11}H_{18}O_2N_2S$, C = 54.5%, H = 7.4%, N = 11.6%).

RESULTS

There was no clinical evidence, in any case studied, of foetal depression attri-

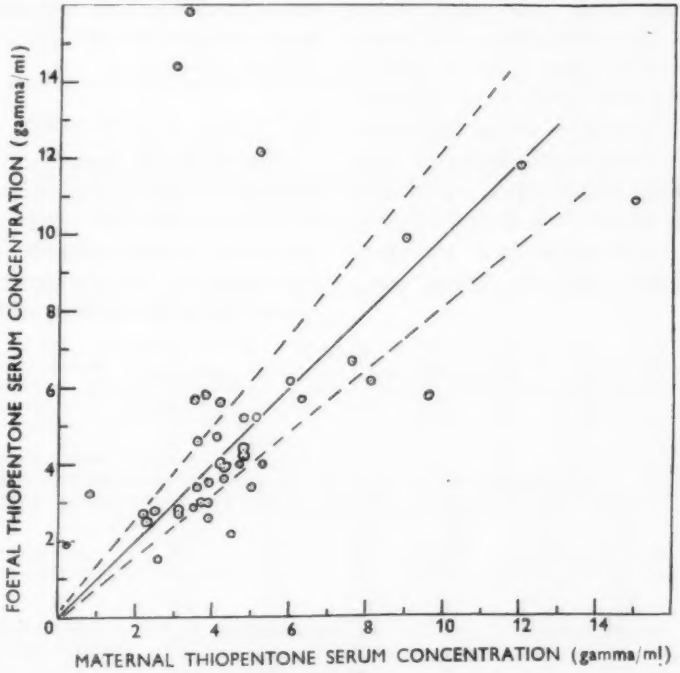

FIG. 2
Relationship between foetal thiopentone level and maternal level at time of clamping cord.
Spaced lines = limits of 10 per cent error

butable to anaesthesia, whatever the length of time between induction and delivery. Moreover, neither the absolute dosage given nor the dosage per kg body weight appeared, within the limits given in table I, to influence the time taken for respiration to commence. The series included cases of prematurity (Nos. 3, 32 and 33), postmaturity (Nos. 4 and 35), foetal distress (Nos. 14, 15, 16, 28, 34 and 35), severe toxaemia of pregnancy (No. 32), and maternal diabetes (No. 33), and again it must be emphasized that these were representative of larger groups of similar cases dealt with previously.

Figure 2 shows the relationship between the foetal and maternal levels at the time of clamping the cord. This graph shows quite clearly that throughout the whole range of operation times given in table I (3–30 min) the two levels were approximately equal. Figure 3 shows the variation of foetal level with lapse of time between finishing the injection and clamping the cord. There is a definite fall in foetal level with time and statistical analysis indicates that the fall is exponential.

From table I it is clear that a significant concentration of thiopentone is built up in the amniotic fluid during delivery, in periods up to 17 minutes. The significance of this finding is outside the scope of this paper.

The results for the volunteer series shown in table II, indicate that no striking correlation between serum thiopentone level and depth of anaesthesia is revealed with the small number of subjects studied. However, it is probably significant that the serum levels at time of awakening for 7 out of the 12 subjects were in the range 6 to 10 gamma/ml. Moreover, all were awake by the time the serum level had fallen to 6 gamma/ml. It seems probable that a study of a much larger number of subjects would reveal a definite correlation.

DISCUSSION

The data of figure 2 indicate that there is no appreciable placental barrier to thiopentone, the drug reaching the foetus at a rate probably depending on the maternal circulation time. This is corroborated by the data of figure 3 which

TABLE II
Thiopentone levels at time of awakening

	Case	Sex	Weight (kg)	Dose (mg)	Dose/Wt (mg/kg)	2 min thio. level (gamma/ml)	5 min level (gamma/ml)	10 min level (gamma/ml)	Time asleep (min)	Interpolated level on waking (gamma/ml)
1	N.H.B.	(F)	62.3	219	3.52	7.2	7.5	17 min. level —	2½	7.3
2	E.B.	(M)	82.7	202	2.68	6.0	7.4	—	2	6.0
3	M.R.McD.	(F)	66.4	223	3.36	7.5	7.7	—	4	7.6
4	C.W.G.	(M)	73.6	225	3.06	14.7	9.5	—	2	14.7
5	F.X.B.	(M)	71.8	226	3.15	16.0	4.2	—	¼	>16
6	E.C.	(F)	51.4	212	4.12	9.1	7.6	—	2	9.1
7	A.V.E.D.	(F)	45.5	227	5.0	9.5	12.4	10.0	10	10.0
8	A.M.D.	(M)	79.1	214	2.71	9.5	8.3	—	5	8.3
9	I.B.D.	(M)	80.0	196	2.45	9.6	4.9	—	1	>9.6
10	M.A. le C.H	(F)	57.3	253	4.41	(85)	(16.4)	—	5	16.4
11	E.M.R.	(M)	78.2	213	2.72	20.2	11.7	4.9	8¼	6.5
12	D.G.W.	(M)	73.2	213	3.91	14.4	8.0	—	1½	>14.4

TABLE I

Clinical and laboratory data

Case No.	Type of and indication for operation	Maternal weight (kg)	Dose of thiopentone (mg)	Dose per kg (mg)	Sample "A" thiopentone gamma per ml serum	Sample "B" thiopentone gamma per ml serum	Sample "C" thiopentone gamma per ml serum	Time from end of injection to clamping cord (min)
1	F.D. Delay in labour (50 hours) deep transverse arrest	70	242	3.46	8.1	4.3	3.9	14
2	L.S.C.S. & sterilization. Disproportion—previous C.S.	66.4	258	3.89	12.4	9.6	5.8	10
3	L.S.C.S.—A.P.H. from placenta praevia	65.5	201	3.07	10.6	3.9	2.6	17
4	F.D. Delay 2nd stage, poor contraction, primigravida	66.4	223	3.36	11.5	6.0	6.2	5
5	F.D. Delay 2nd stage, primigravida	71.8	234	3.26	5.8	5.2	12.2	4
6	L.S.C.S. Elderly primigravida with toxaemia and thyrotoxicosis	64.5	216	3.35	4.9	0.7	3.2	17
7	F.D. Delay 2nd stage, primigravida	76.0	230	3.03	9.3	3.7	3.0	16
8	F.D. Transverse lie, delay 2nd stage, primigravida	77.3	261	3.38	12.2	3.6	3.4	10
9	F.D. Delay 2nd stage, some foetal distress	86.8	259	2.98	8.9	3.1	2.8	25
10	L.S.C.S. Uterine inertia, foetal distress	79.1	224	2.83	16.0	4.7	4.0	7
11	L.S.C.S. Two previous C.S., foetal distress. A.P.H., mother Rh-negative	60.5	211	3.49	11.0	3.9	3.0	30
12	F.D. Inertia, exhausted, primigravida	73.2	217	2.87	6.1	2.3	2.5	8
13	F.D. Prolonged labour, primigravida, persistent posterior presentation	74.5	224	3.01	4.9	0.2	1.9	23
14	F.D. Foetal distress	76.8	217	2.82	2.0	3.0	14.4	6
15	F.D. Foetal distress	74.1	211	2.85	2.6	2.6	1.5	7
16	F.D. Foetal distress	95.0	213	2.29	6.7	3.6	4.6	7
17	F.D. No progress 2nd stage, posterior position, primigravida	65.0	221	3.74	6.2	3.1	2.7	8
18	F.D. No advance 2nd stage, gynaecoid pelvis	63.4	234	3.68	5.6	5.1	5.2	8
19	F.D. Delay 2nd stage, some foetal distress	65.5	227	3.47	6.7	3.5	5.7	10
20	F.D. Delay 2nd stage, elderly primigravida	64.5	221	3.42	6.6	4.8	5.2	9
21	F.D. No advance, foetal heart slowing, primigravida	82.7	225	2.60	6.7	4.2	5.6	9
22	L.S.C.S. Pelvic contraction, two previous C.S.	51.4	211	4.11	16.3	15.0	10.9	11
23	F.D. Idiopathic megalocardia, 1 hour in 2nd stage, not in failure	85.0	251	2.95	8.1	6.3	5.7	6
24	F.D. No advance, primigravida	74.1	227	3.06	10.0	5.3	4.0	12
25	F.D. Prolonged labour, some uterine inertia, transverse lie, difficult delivery	65.9	240	3.64	7.0	3.3	15.8	20
26	F.D. No advance, some foetal distress	59.5	239	4.01	9.1	9.0	9.9	3
27	F.D. Delay 2nd stage	66.4	240	3.62	17.9	12.0	11.8	4
28	F.D. No advance, some foetal distress	60.5	235	3.04	13.6	7.6	6.7	4
29	F.D. Delay. Persistent posterior position, primigravida	76.8	215	2.80	6.0	2.5	2.8	19
30	F.D. Maternal distress, No advance	67.3	180	2.68	8.3	4.3	3.6	15
31	F.D. Deep transverse arrest	77.7	237	3.05	8.0	4.8	4.4	12
32	L.S.C.S. Very bad toxaemia, no fits	89.1	210	2.04	13.2	4.5	2.2	13
33	L.S.C.S. Diabetes, hypertension with oedema, previous C.S.	62.3	240	3.85	13.7	5.0	3.4	15
34	F.D. Foetal distress	60.5	153	2.53	11.9	8.1	6.2	10
35	F.D. Foetal and maternal distress	94.1	200	2.13	6.4	4.2	4.0	6
36	L.S.C.S. Foetal distress, A.R.M. revealed heavy meconium staining	73.2	218	2.98	5.0	4.1	4.7	13
37	F.D. Maternal distress, slowing foetal heart	80.0	206	2.575	7.4	4.8	4.2	6
38	F.D. Maternal distress, impending inertia	80.5	221	2.75	8.3	3.5	2.9	12
39	L.S.C.S. Contracted pelvis, brow presentation	64.1	241	3.75	7.3	2.2	2.7	17
40	F.D. Gross maternal distress	77.3	233	3.0	7.9	3.8	5.8	8
41	F.D. Maternal distress	61.8	201	3.36	6.4	3.9	3.5	6

Notes: In column 2: F.D.=Forceps delivery. L.S.C.S=Lower segment Caesarean section. A.P.H.
Sample "A"=Maternal serum 2 minutes after completion of injection of thiopentone. S

TABLE I

nd laboratory data on 41 cases

Sample "C" thiopentone gamma per ml serum	Time from end of injection to clamping cord (min)	Time from clamping the cord to first cry (min)	Condition at birth	Resuscitative measures	Weight of infant (kg)
3.9	14	On delivery	Excellent	None	4.0
5.8	10	6	Slow to breathe, much mucus	1 ml lobeline into cord, immediate response	3.0
2.6	17	Less than 1	Excellent	Nasal oxygen	2.1
6.2	5	During delivery	Excellent	None	4.1
12.2	4	Less than 1	Excellent	Short spell nasal oxygen	2.9
3.2	17	Less than 1	Excellent	None	3.1
3.0	16	Less than 1	Excellent	None	2.9
3.4	10	1	Excellent	Short spell nasal oxygen	3.8
2.8	25	Less than 1	Excellent	None	3.1
4.0	7	On delivery	Excellent	None	3.1
3.0	30	1	Good but relapsed lethargic, jaundiced, weak	Nasal oxygen, later oxygen tent	2.8
2.5	8	1	Excellent	Short spell nasal O_2	3.7
1.9	23	5	Whimpered in 1 min excellent in 5 min	Nasal oxygen	3.6
14.4	6	On delivery	Excellent	None	3.7
1.5	7	Less than 1	Excellent	Short spell nasal O_2	3.2
4.6	7	4	Gasped in 1 min, rather limp, cried well 4 min	5–6 min nasal oxygen	3.9
2.7	8	Less than 1	Excellent	None	4.0
5.2	8	On delivery	Excellent	None	3.44
5.7	10	On delivery	Excellent	None	3.16
5.2	9	Less than 1	Good	Short spell nasal O_2	2.98
5.6	9	On delivery	Excellent	None	3.3
10.9	11	1	Good	Nasal oxygen	3.24
5.7	6	On delivery	Excellent	None	3.95
4.0	12	On delivery	Rather limp, much moulding of head	Short spell nasal O_2	3.95
15.8	20	20	Poor, asphyxia livida	Endotracheal & gastric O_2 nikethamide 0.5 mg 1 min good recovery	3.86
9.9	3	2	Good	Nasal oxygen	3.75
11.8	4	On delivery	Excellent	None	4.4
6.7	4	Less than 1	Excellent	None	3.55
2.8	19	On delivery	Excellent	None	3.95
3.6	15	2	Rather limp for 1 min	Short spell nasal O_2	3.81
4.4	12	On delivery	Excellent	None	3.86
2.2	13	On delivery	Excellent	None	1.85
3.4	15	10	Gasped strongly on delivery but no further response	Nikethamide 0.5 ml into cord, 0.5 ml 1 min nasal O_2 good recovery	3.12
6.2	10	On delivery	Excellent	None	3.47
4.0	6	2–3	Fair, rather limp, much meconium staining	Nasal oxygen	3.52
4.7	13	4	Much meconium staining, breathing well in 1 min	Nasal oxygen	3.55
4.2	6	On delivery	Excellent	None	2.98
2.9	12	On delivery	Excellent	None	3.1
2.7	17	Less than 1	Excellent	Very short spell nasal oxygen	3.64
5.8	8	On delivery	Excellent	None	3.55
3.5	6	1	Good	Short spell nasal O_2	3.61

section. A.P.H. = Antepartum haemorrhage. A.R.M. = Artificial rupture of membranes.
of thiopentone. Sample "B" = Maternal serum at time of cutting cord. Sample "C" = Foetal serum at time

	Weight of infant (kg)	Amniotic thiopentone concentration (gamma)	Week of pregnancy
	4.09	—	40
to cord,	3.04	1.2	39
ise			
	2.12	—	32
	4.12	—	43
	2.92	—	40
	3.12	0.55	38
	2.9	—	40
	3.82	—	40
	3.10	—	40
	3.18	—	40
er	2.85	—	36
O_2	3.72	—	40
	3.69	—	40
	3.75	—	41
O_2	3.27	—	42
gen	3.95	—	41
	4.03	—	40
	3.44	—	40
	3.16	—	42
O_2	2.98	—	40
	3.3	—	40
	3.24	3.9	40
	3.95	—	40
O_2	3.95	—	41
stric	3.86	—	42
5 mg			
ery			
	3.75	—	42
	4.4	—	40
	3.55	—	40
	3.95	—	42
O_2	3.81	—	40
	3.86	—	42
	1.85	0.05	31
l into	3.12	0.3	35
overy			
	3.47	—	40
	3.52	—	43
	3.55	—	42
	2.98	—	41
	3.1	—	41
	3.64	—	36
	3.55	—	43
	3.61	—	40

m at time of cutting cord.

indicates that the foetal level is at a maximum virtually at the onset of anaesthesia and thereafter falls, presumably at a rate determined by the combined foetal and maternal metabolism, redistribution and excretion. There is, therefore, no point in adhering to a five-, ten- or twelve-minute rule, and with the single dose anaesthetic procedure, as described in Part IV, thiopentone may be used no matter what length of time delivery may take. Indeed, the longer the time interval between injection of thiopentone and delivery of the child, the lower are the foetal thiopentone levels and, presumably, the less the likelihood of difficulty in starting foetal respiration. As was stated above, Hellman et al. gave no indication of their administration technique and it is probable that with continuous or multiple injection techniques, the foetal thiopentone serum levels will rise in parallel with the maternal serum levels, with increasing lapse of time between commencement of anaesthesia and clamping the cord.

It is of interest to refer here to the statement by Walker (1954) that in many cases of postmaturity and of some deliveries occuring at term, the foetus is balancing on the brink of anoxia. During the induction period of most general anaesthetics the maternal oxygen supply is impaired and, if there is difficulty in induction, and maternal cyanosis occurs,

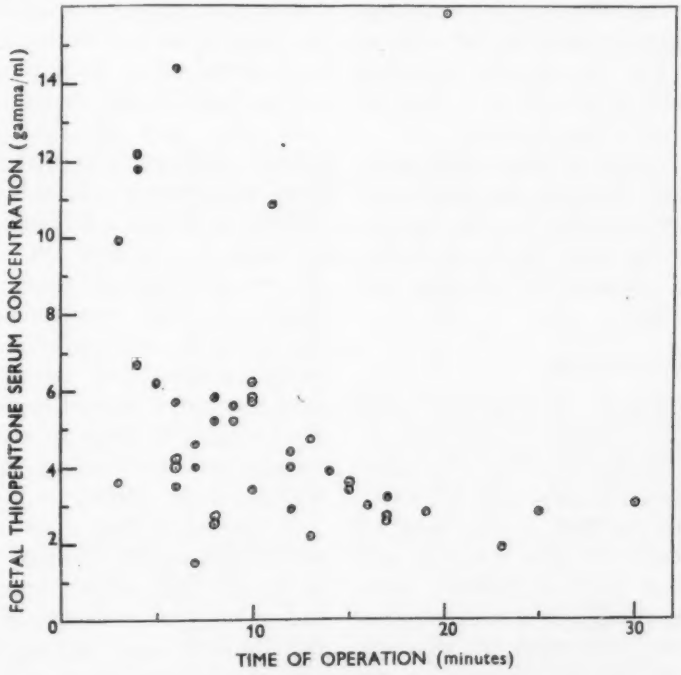

FIG. 3
Variation of foetal thiopentone level with time of operation.

very little oxygen would be transferred to the foetus. It is contended here that using thiopentone, difficulties of induction are minimal, and that maternal and foetal oxygenation is maintained throughout anaesthesia.

Statistical analysis of results.

The trend of data of figure 2 was so self-evident that statistical analysis was beside the point.

In the case of figure 3, for theoretical reasons it seemed valid to correlate log (foetal serum level) against time rather than the foetal serum level itself against time. When this is done −0.41 correlation is obtained with 41 pairs. Upon taking those results obtained from patients receiving dosages between (*a*) 200–230 mg and (*b*) 2.75–3.25 mg/kg, the following correlations were obtained: (*a*) −0.38 for 24 pairs; (*b*) −0.54 for 16 pairs.

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As was noted above, the actual time of cessation of placental transmission was of vital interest in the estimation of foetal thiopentone levels at time of delivery. A second point of interest concerned the technique, as described in Part IV, of ceasing the administration of any cyclopropane which was being used and increasing the oxygen to a maximum, just as the foetal head was crowned. This would be a wasted effort if the placental transmission had already ceased.

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minutes should mitigate against the use of thiopentone as an induction agent.

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THE use of relaxant drugs in obstetric anaesthesia is a practice which appears gradually to have grown without any accompanying attempt to define precisely the indications for their employment. Roughly, there are two objectives: (1) to obtain muscular relaxation at the site of surgical manoeuvre; (2) to facilitate intubation under light anaesthesia. The latter objective is related to the question of vomiting and is discussed in Part III of this article.

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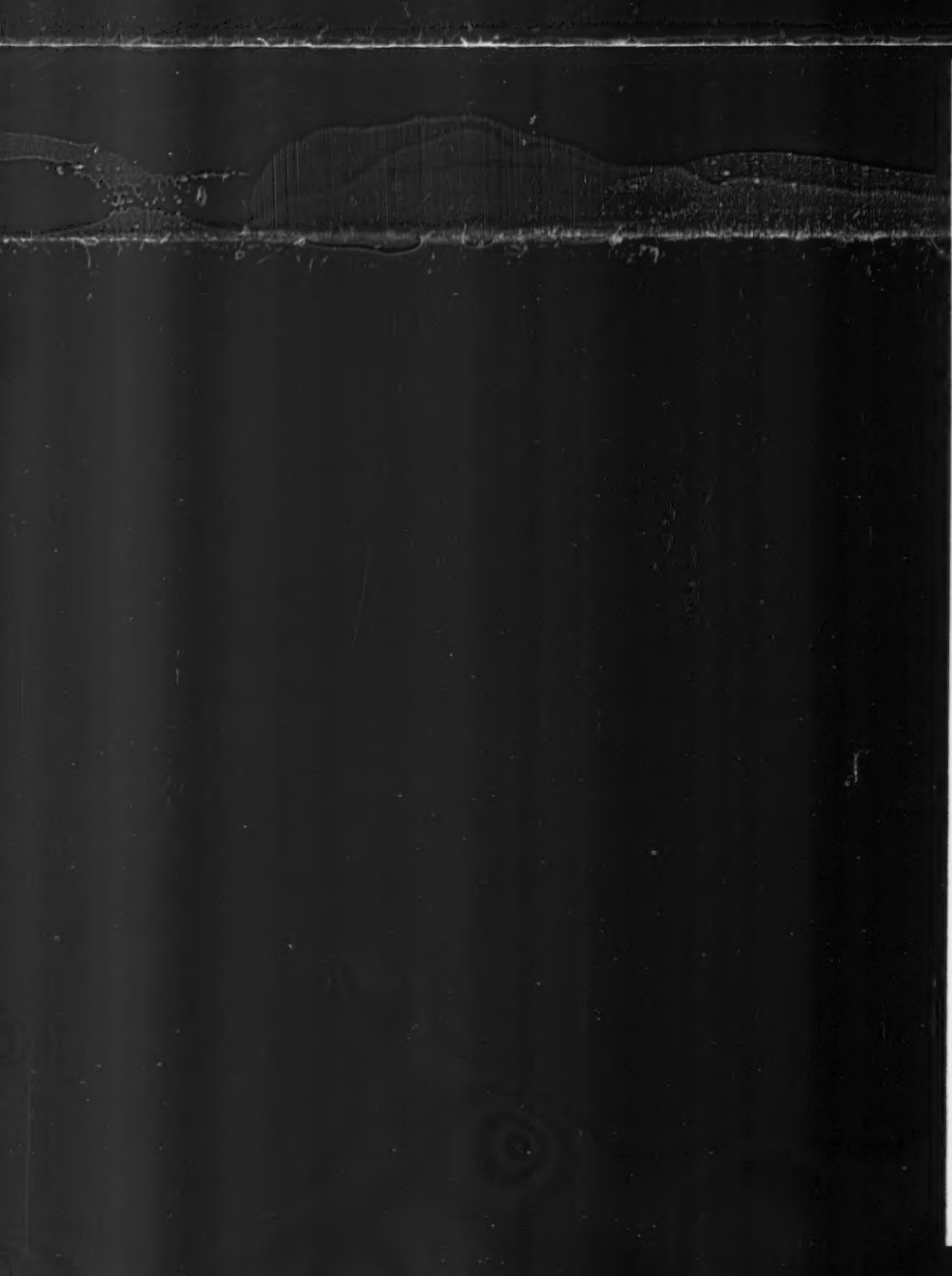

indicates that the foetal level is at a maximum virtually at the onset of anaesthesia and thereafter falls, presumably at a rate determined by the combined foetal and maternal metabolism, redistribution and excretion. There is, therefore, no point in adhering to a five-, ten- or twelve-minute rule, and with the single dose anaesthetic procedure, as described in Part IV, thiopentone may be used no matter what length of time delivery may take. Indeed, the longer the time interval between injection of thiopentone and delivery of the child, the lower are the foetal thiopentone levels and, presumably, the less the likelihood of difficulty in starting foetal respiration. As was stated above, Hellman et al. gave no indication of their administration technique and it is probable that with continuous or multiple injection techniques, the foetal thiopentone serum levels will rise in parallel with the maternal serum levels, with increasing lapse of time between commencement of anaesthesia and clamping the cord.

It is of interest to refer here to the statement by Walker (1954) that in many cases of postmaturity and of some deliveries occuring at term, the foetus is balancing on the brink of anoxia. During the induction period of most general anaesthetics the maternal oxygen supply is impaired and, if there is difficulty in induction, and maternal cyanosis occurs,

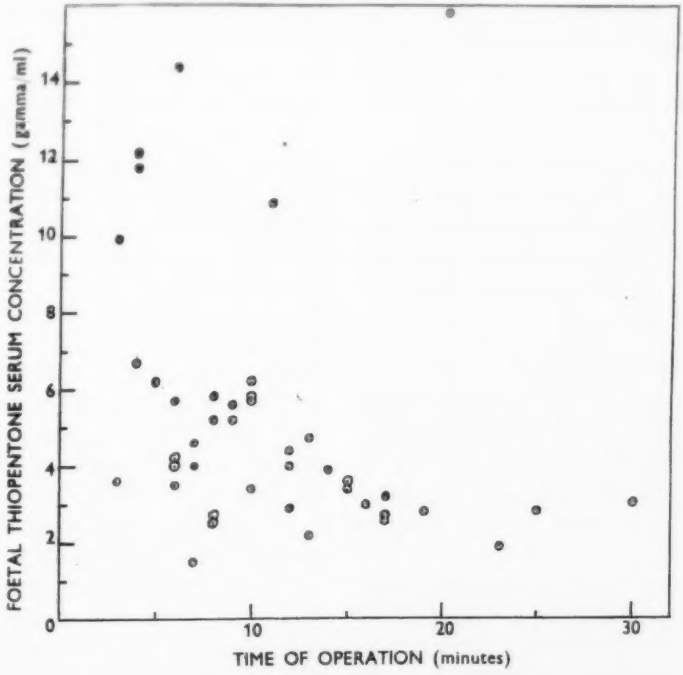

FIG. 3
Variation of foetal thiopentone level with time of operation.

very little oxygen would be transferred to the foetus. It is contended here that using thiopentone, difficulties of induction are minimal, and that maternal and foetal oxygenation is maintained throughout anaesthesia.

Statistical analysis of results.

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However, for Caesarean section, and to a lesser extent for forceps delivery, it has become the practice of increasing numbers of anaesthetists to use relaxant drugs.

An obvious danger, early appreciated, is the possibility of placental transmission of the relaxant, leading to a degree of neonatal paralysis. However, following the initial work of Gray (1947), who demonstrated that d-tubocurarine did not appear in the foetal blood, a number of authors confirmed the absence of clinical effects on the child when d-tubocurarine was given to the mother (Whitacre and Fisher, 1948; Corbett and Thomas, 1949; Climie, 1950; Davenport, 1951; Austin and Mering, 1951). None of the latter group of authors substantiated their clinical impressions by analysis of the cord blood.

Apgar and Papper (1952) in their survey of placental transmission, in which the only relaxants discussed were d-tubocurarine and decamethonium, confined themselves to recording that their general impression was that the drugs were not transmitted. Thomas and Gibson (1953) reported similar findings with d-tubocurarine, dimethyl d-tubocurarine, decamethonium and gallamine; again no blood analyses were undertaken. Jewell (1954) in an account of the use of decamethonium for forceps delivery stated that "it is reported that these curare-like drugs do not cross the placenta".

Cohen et al. (1953), in an analysis of nine cases, demonstrated that no d-tubocurarine (Intocostrin) passed through the placenta when doses ranging from 18 to 42 units had been administered to the mother. Somewhat earlier, Pittinger and Morris (1953) had found that d-tubocurarine, when injected in large doses, directly into the uterine artery of pregnant bitches, was transmitted to the placenta to some extent.

The three drugs probably most commonly used in this country to produce relaxation are d-tubocurarine, gallamine, and suxamethonium. The work described below is an investigation into the occurrence of placental transfer of the first two of these drugs.

METHOD

(a) *Clinical.*

Each patient was given either gallamine triethiodide (80 mg) or d-tubocurarine chloride (15 mg or 20 mg) immediately after induction with thiopentone. No test dose was given. Maternal serum samples "A" and "B" and cord serum sample "C" were obtained as in the thiopentone investigation and a pre-operative maternal sample was also taken.

(*b*) *Biological assay of gallamine and d-tubocurarine.*

Gallamine and d-tubocurarine were assayed by a method similar to that of de Jalon (1947) in which the drug antagonizes the acetylcholine contracture of the frog's rectus abdominis. Oxygen and CO_2 were used for aeration, relaxation of the muscle was assisted by electrical stimulation and the timing of operations was automatically performed: with these modifications an increase in sensitivity of 4–5-fold was obtained.

One-half of the longitudinally divided muscle was immersed in a frog Ringer solution (NaCl 6 g/l., KCl 0.15 g/l., $CaCl_2.6H_2O$ 0.3 g/l., $NaHCO_3$ 0.5 g/l.) at room temperature (*c.* 20°C) and aerated with 95% O_2 + 5% CO_2. The assay cycle

was controlled by an automatic apparatus of the type described by Boura et al. (1954) with automatic addition of the constant dose of acetylcholine (usually 0.3 ml of 10^{-5} *M* solution acetylcholine perchlorate in frog Ringer solution). Relaxation of the muscle after the contracture was aided by a period of electrical stimulation, applied by electrodes at the top and bottom of the bath. Capacitor discharges (1/sec) produced twitches, the rebound of the gimbal lever producing the necessary gentle stretching of the muscle. The cycle of events was thus: (1) manual replacement of bath contents with antagonist solution (4 ml); (2) after 2 minutes, addition of acetylcholine; (3) 90 seconds exposure; (4) two complete washes; (5) 30 seconds electrical stimulation; (6) 90 seconds rest.

Initially, the solutions to be assayed were prepared free of protein by dialysis of the serum against a larger volume of frog Ringer solution, since the frothing, which resulted if serum were added directly to the bath contents, interfered with the assays. Later it was found that the froth could be controlled by the presence of the silicone material M.S. antifoam A, held in the liquid surface throughout the experiment by placing a small amount on the needle introducing the acetylcholine; no deleterious effects on the responses of the muscles were seen. The effects of alternate doses of the serum to be assayed and standards, containing pre-operative serum plus added drug,

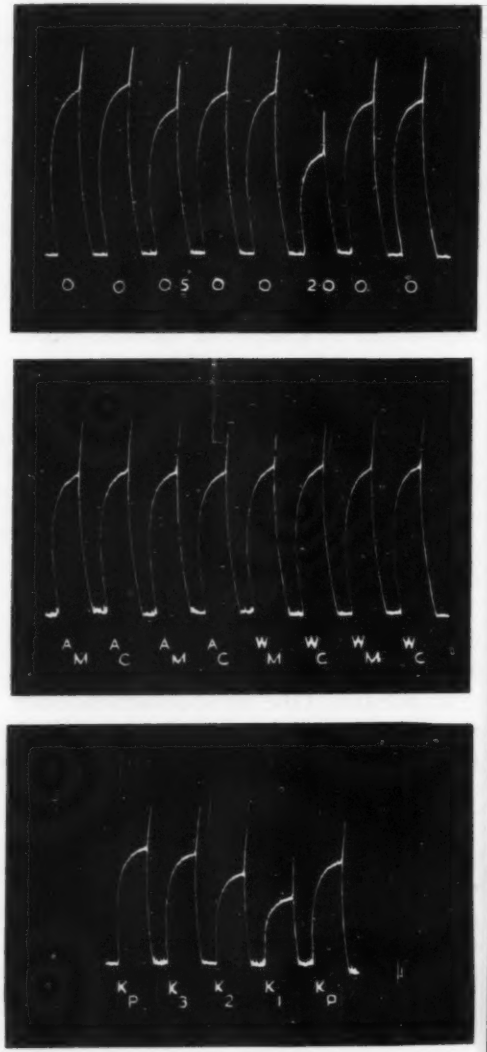

FIG. 4

(A) Responses of the frog rectus abdominis preparation to a constant dose of acetylcholine when the antagonist solution contained 0, 0.5, 2.0 μg gallamine triethiodide as indicated below the tracing.

(B) Responses obtained when the antagonist solution contained alternately 0.2 ml of maternal serum (A_m, W_m) or cord serum (A_c, W_c) obtained from two normal deliveries.

(C) Comparison of responses in the presence of 0.2 ml of serum samples from a case receiving gallamine. K_p pre-operative, K_1 first maternal, K_2 maternal at delivery, K_3 cord sample.

were compared. A final estimate was made proportionately from the two standards most closely straddling the unknown. Normally the amounts of drug contained in the 4 ml of antagonist solution were 0.05–0.30 μg d-tubocurarine chloride, or 0.5–3.0 μg of gallamine triethiodide. Fig. 4A shows the responses obtained when the antagonist solution contained 0.5 or 2.0 μg gallamine triethiodide. The volume of the antagonist solution needed to be carefully measured since the preparation was particularly sensitive to changes in the acetylcholine concentration. Over the midportion of the range standards differing by 10 per cent could be used to straddle the unknown, but doses differing by 20 per cent were more common.

The preparation would usually tolerate a maximum of 0.2 ml serum/4 ml solution; Fig. 4B shows the responses recorded in the presence of 0.2 ml of maternal or cord serum from two normal deliveries. Fig. 4C compares the effects of the preoperative sample with those of the later three samples in a case in which gallamine was used.

RESULTS

Nineteen cases were investigated; 13 received gallamine and 6 d-tubocurarine. None of the infants appeared to be affected by either drug. The mothers were not rendered apnoeic by the dosage of relaxant used, there was no difficulty in their general anaesthetic management. The laboratory results are recorded in table IV.

TABLE IV
Transmission of relaxant drugs

Case No.	Maternal weight (kg)	Dose mg/kg	μg/ml serum Sample "A"	Sample "B"	Sample "C"	Time induction to delivery (min)
		Gallamine triethiodide (dose 80 mg)				
3	65.5	1.22	8.0	4.8	2.0	17
6	64.5	1.24	2.5	1.8	1.7	17
10	79.1	1.01	8.5	7.5	(Just over) (1.0)	7
22	51.4	1.55	13.5	5.0	1.0	11
29	76.8	1.04	4.0	1.0	1.0	19
31	77.7	1.03	4.0	3.0	3.0	12
32	89.1	0.90	10.0	7.0	1.0	13
33	62.3	1.29	12.0	1.5	1.0	15
34	60.5	1.32	20.0	8.0	2.0	10
A	63.6	1.26	6.0	5.0	2.5	9
B	79.6	1.0		5.5	2.5	3
C	76.4	1.05	8.5	8.0	2.0	3½
D	60.5	1.32	14.0	8.0	1.5	5½
		d-Tubocurarine chloride (dose 20 mg)				
35	94.1	0.212	2.5	1.5	<0.5	6
36	73.2	9.273	1.3	1.3	<0.5	13
37	80.0	0.25	2.5	1.8	0.6	6
		d-Tubocurarine chloride (dose 15 mg)				
38	80.5	0.187	2.2	1.8	0.7	12
39	64.1	0.234	1.3	0.6	<0.2	17
40	77.3	0.194	2.2	0.4	0	8

The case numbers coincide with those given in table I. Sample "A" = maternal plasma 2 minutes after time of injection of relaxant.
Sample "B" = maternal plasma at time of delivery. Sample "C" = foetal plasma at time of delivery.

DISCUSSION

In each of the cases which were given gallamine an appreciable concentration of the drug was detected in the cord serum. The amounts found bore no simple relation to the concentration in the maternal serum, neither could the foetal level be related to the dose per unit weight given. There seems almost to be an upper limit to the foetal serum concentration of about 3 μg/ml; this was not exceeded despite the wide variation in dosage (0.90 to 1.55 mg/kg) and in the time elapsing (3–19 minutes) between induction and delivery. The number of cases is too small for this to be definitely established, but it may be that the rate of excretion of the drug by the foetus is sufficient to prevent the foetal serum concentration rising any higher, rather than that there is any limitation on transfer from the mother.

It has been established (Stead, 1955) that infants are more susceptible to the paralysing actions of curare-like drugs than are adults, but whether a serum concentration of 3μg/ml could be clinically significant is not known; none of the infants in this series appeared to be paralysed. It will be seen, however, from table IV that maternal levels of this order were found after ordinary clinical doses of gallamine, and a more sensitive test of neuromuscular block in the infants might show an effect. There is, therefore, the possibility that the use of gallamine might have to be considered as yet another cause of neonatal depression; in which case, the attempted diagnosis and treatment might well lead to considerable confusion.

On the other hand, the cord serum concentrations of d-tubocurarine were all very low, in four cases insufficient amounts being present to permit normal assay. Again the levels could not be directly related to those in the maternal serum or to the time of delivery. It is possible, therefore, to conjecture that clinically significant amounts of the drug are unlikely to be found circulating in the foetal blood.

SUMMARY

Gallamine triethiodide (13 cases) and d-tubocurarine chloride (6 cases) were given during the course of a series of obstetric operations.

The concentration of the relaxant drug in the serum of two maternal and one cord sample in each case, was determined by a bio-assay method.

With equipotent doses of the two drugs, d-tubocurarine appeared in the foetal serum in traces only, while gallamine occurred in readily detectable and possibly significant amounts.

None of the infants involved appeared clinically to be affected by the procedure.

The rationale of the use of relaxant drugs in obstetric anaesthesia is discussed.

ACKNOWLEDGMENT

Our thanks are due to Professor W. D. M. Paton for his helpful advice and discussion throughout the investigations.

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(*To be continued*)

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DUAL ACTION OF SUXAMETHONIUM CHLORIDE

BY

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DURING the last three or four years several cases of prolonged apnoea after suxamethonium chloride have been reported in the medical literature. In some of them the cause of the apnoea was obscure, in others its duration was too short to be of much clinical significance. Among the remainder, however, are a number of well authenticated cases where the apnoea could definitely be attributed to suxamethonium chloride, and a few in which, rather surprisingly, the apnoea was apparently reversed by neostigmine (Hamer Hodges, 1953, 1955; Argent et al., 1955). Personal interest in this condition was stimulated by the following case:

A.G., age 62 years, a short, heavily built woman of 11½ stone (73 kg), was admitted to hospital at 3 a.m. complaining of abdominal pain of 36 hours duration. Temp. 100.6°, P.R. 112, Resp. 26. Her symptoms were of an atypical acute abdomen, and conservative treatment was adopted. Twelve hours later the diagnosis was still uncertain but it was decided that laparotomy must be performed. Premedication: papaveretum 20 mg, hyoscine 0.4 mg.

P.M.

5.0	Induction: 400 mg thiopentone followed by 50 mg suxamethonium chloride. Apnoea resulted and a No. 10 cuffed endotracheal tube was passed. Spontaneous respiration rapidly returned. Anaesthesia maintained with nitrous oxide (6 litre per minute flow), oxygen (2 litre), by "semi-open" method with no carbon dioxide absorption.
5.10	Operation begun; 80 mg gallamine.
5.10–5.20	Apnoea. Controlled respiration.
5.20–5.30	Aided respiration.
5.30–5.40	Spontaneous respiration. Operation revealed a gangrenous appendix with free purulent fluid in the peritoneal cavity.
5.40	The surgeon was about to close the peritoneum and complained of the tightness of the abdomen. 75 mg suxamethonium chloride. Apnoea resulted and persisted at the end of operation.

I first saw the patient about 9.30 p.m.—nearly four hours later. During this period adequate pulmonary ventilation had been maintained with the same flows of nitrous oxide and oxygen, but no other treatment had been given. She was no longer apnoeic but aided respirations were still essential, her own—18 per minute—being extremely shallow and quite inadequate. Faradic stimulation of the ulnar nerve 2 inches above the internal condyle of the humerus elicited only a feeble response. A sample of alveolar air collected in a vacuum chamber via a polythene tube passed down to the carina was found on analysis (Haldane) to contain oxygen 19.5 per cent, carbon dioxide 5.45 per cent. A sample of venous blood was collected for estimation of serum cholinesterase; the value later determined by the method advocated by de la Heurga et al. (1952) was 260 micromoles (normal, 130–310 micromoles).

P.M.

9.50	Respirations were perhaps a little deeper, but were still quite inadequate. It was thought that the suxamethonium chloride was almost certainly the cause of her depression, and with the idea of determining whether it was still acting as a depolarizing agent or had become a competitive blocker, and whether in consequence neostigmine would make matters worse or better, the patient was given 10 mg gallamine. This immediately caused a marked further reduction of pulmonary ventilation, the patient again becoming almost apnoeic.
10.20	As far as could be judged, her respirations had now recovered to approximately the same depth as before the administration of the 10 mg gallamine at 9.50 p.m., though they were still so shallow that to discontinue assisting them was quite out of the question. 1 mg atropine sulphate.
10.25	1 mg neostigmine.
10.30	0.75 mg neostigmine.
10.34	0.75 neostigmine.
	} Very marked increase in depth of respiration.
10.40	No aided respiration required. Nitrous oxide discontinued. Extubation.

10.50 Patient conscious and talking. Returned to ward.

Her subsequent convalescence was uneventful and she was discharged on the fourteenth day after operation.

In this case happily the picture was not obscured by a multiplicity of drugs, and it was difficult to believe that the prolonged apnoea yielding later to very shallow respiration was due to any factor other than the suxamethonium chloride. The increased paralysis caused by gallamine and the antidotal effect of neostigmine suggested that the suxamethonium chloride had changed its action to that of a competitive blocking agent.

Paton (1953) stated that with some drugs and in some animals, the neuromuscular block produced by certain compounds did not fall clearly into the category of either a competitive or a depolarizing mechanism, but appeared to represent an action corresponding to a mixture of the two, the transition always being in the direction from a depolarizer to a d-tubocurarine-like drug. Zaimis (1953) suggested that in monkeys, rabbits, hares, and dogs, decamethonium and suxamethonium exhibited a dual mode of action. She considered that their action began by depolarizing but changed during the blocking process to competition with acetylcholine. Gray (1954) stated that a dual action of suxamethonium chloride had not been observed in man, but Churchill-Davidson (1955) thought that possibly in certain circumstances a dual type of block might occur in normal subjects after a depolarizing drug had been given.

The observations reported in this paper suggest that in man a transition from a depolarizing to a competitive—or, the term preferred by Foldes (1954)—an antidepolarizing effect, regularly occurs in patients who are given suxamethonium chloride by drip infusion during operation.

Apart from their different responses to electrical stimuli, there are three main methods of distinguishing a depolarizing from an antidepolarizing block in man:

(1) The presence or absence, of fasciculation.
(2) Reversibility by neostigmine.
(3) Interaction with other relaxants.

FASCICULATION

The statement made by several writers that fasciculation invariably occurs after the administration of suxamethonium chloride, is not, of course, strictly accurate. Fasciculation does not follow the administration of suxamethonium chloride to patients who have recently received normal clinical doses of competitive blocking agents, e.g. it never occurs when suxamethonium chloride is given to facilitate closure of an abdomen that has previously been relaxed by d-tubocurarine or gallamine.

In order to gain some idea of the amount of a competitive blocking agent needed to avert fasciculation, 10 mg gallamine mixed with 300–400 mg thiopentone were injected intravenously into each of fifty patients, and followed by 50 mg suxamethonium chloride. Fasciculation could be detected in only six of the fifty, and in them it was very slight. This observation coupled with the apparent alteration in the mode of action of suxamethonium chloride reported later in this paper, suggests a possible explanation of the rather puzzling fact that if this drug is given in

repeated doses, even at twenty minute intervals, fasciculation rarely follows the second and subsequent injections. It may be that when suxamethonium chloride is administered in this way, fasciculation is averted by the presence at the myoneural junctions of a small amount of a competitive blocking agent derived from the initial dose of this depolarizing drug.

REVERSIBILITY BY NEOSTIGMINE

Since the experimental work of Longo (1949) Castillo and de Beer (1950) and Bovet et al. (1951), it has been accepted that far from being an antidote to suxamethonium chloride, neostigmine potentiates its action—prolonging, but not increasing the paralysis it causes. This effect is demonstrated clinically in figure 1 which records on the same patient the effect on pulmonary ventilation produced by (*a*) 10 mg suxamethonium chloride, (*b*) 10 mg suxamethonium chloride preceded by 2 mg neostigmine.

Alterations in pulmonary ventilation were regarded as the most satisfactory index of changes in the degree of neuromuscular block. At the start of these investigations, an attempt was made to record such alterations by a pneumograph strapped round the patient's chest. It soon became apparent that tracings obtained in this way were sometimes grossly misleading, so this technique was abandoned. Instead the reservoir bag of a Boyle's machine was inserted through the neck of a sealed aspirating bottle which was connected by wide bore tubing to a recording spirometer. This method proved very satisfactory and can be recommended (plate I).

In contrast to the effect shown in figure 1 of neostigmine potentiating the action of a small dose of suxamethonium chloride, it was found that when a patient had

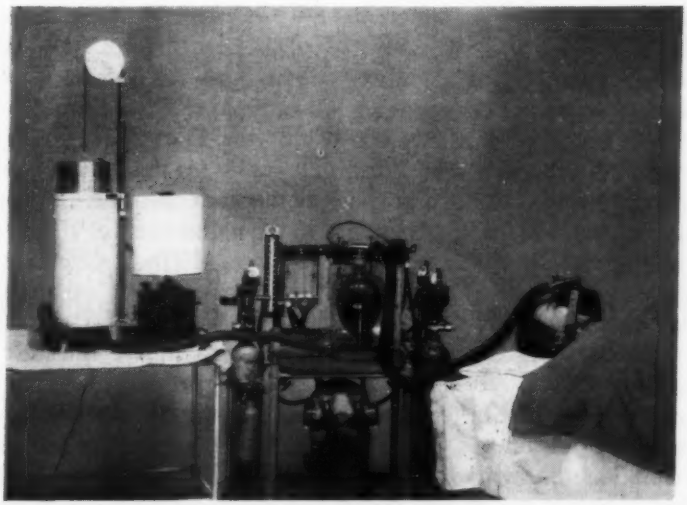

PLATE I

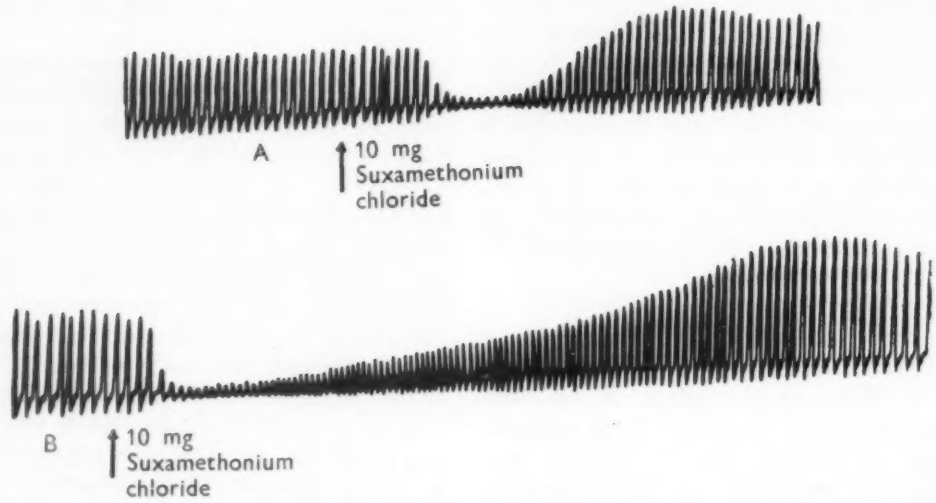

FIG. 1

A. Effect of 10 mg suxamethonium chloride on pulmonary ventilation.
B. Effect of 10 mg suxamethonium chloride in the same patient 4 minutes after she had been given 2 mg neostigmine preceded by 1 mg atropine sulph.

been relaxed throughout operation by a drip infusion of this drug, neostigmine usually acted as an antidote. Twenty-five patients who had received amounts of suxamethonium chloride varying from 150 to 950 mg in a 0.1 per cent solution by drip infusion over periods ranging from half to two hours, were each given 2 mg neostigmine preceded by 1 mg atropine, the drips being continued at the same rate as before. In three patients, little effect was seen. In the remaining twenty-two, there was a definite reversal of paralysis as shown by increased pulmonary ventilation (fig. 2). In sixteen of the twenty-two, this reversal was maintained; in six it was only temporary and after about two minutes the pulmonary ventilation became less than before the neostigmine was administered (fig. 3). These six patients had all received relatively small amounts of suxamethonium chloride.

Interaction with Gallamine.

It is generally accepted that substances having a depolarizing action are antagonistic to those acting by competitive inhibition (Gray, 1954). Figure 4 shows clinically (a) depression from 8 mg suxamethonium chloride, (b) depression from 40 mg gallamine, (c) 30 minutes later, the result of 40 mg gallamine immediately followed by 8 mg suxamethonium chloride. Figure 5 shows the effect of 20 mg suxamethonium chloride on another patient depressed by 80 mg gallamine. It was found, however, that like neostigmine, gallamine caused very different effects on patients who had received small doses of suxamethonium chloride and on those who had been given larger amounts by drip

FIG. 2

Typical effect of 2 mg neostigmine on patient who had been on a suxamethonium infusion for 1 hour. Approx. 350 mg.

FIG. 3

Less common result of 2 mg neostigmine on patient who had been on suxamethonium infusion, viz. increase in pulmonary ventilation, changing to a decrease. (Inspiration downwards.)

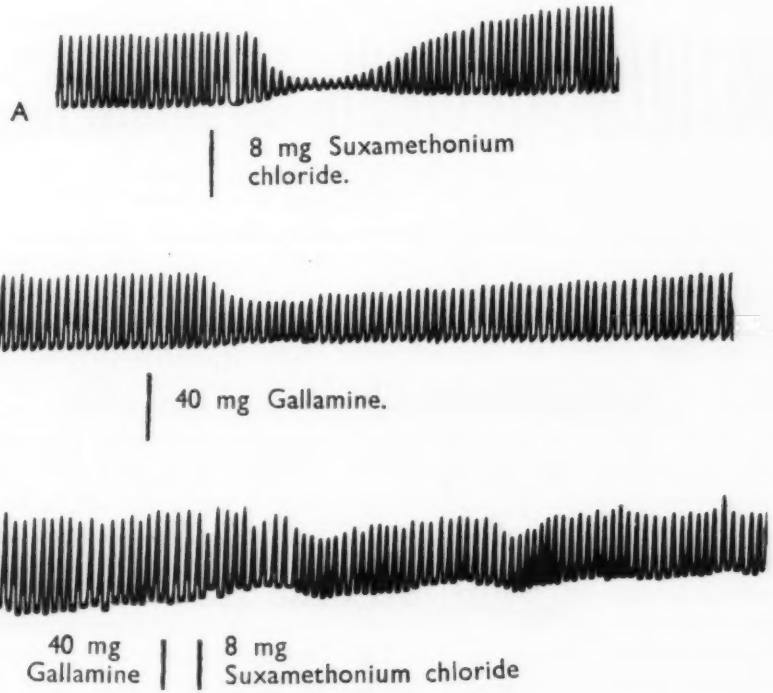

FIG. 4

A. Effect of 8 mg suxamethonium chloride.
B. Effect of 40 mg gallamine.
C. Effect of 40 mg gallamine immediately followed by 8 mg suxamethonium chloride.

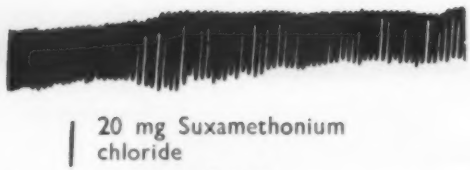

FIG. 5
Effect of 20 mg suxamethonium chloride on patient who had received 80 mg gallamine 15 minutes previously.

infusion. Twenty-two patients to whom suxamethonium chloride had been administered throughout operation by drip infusion were each given 10 mg gallamine. In every case this very small dose of gallamine resulted in a definite, and sometimes dramatic, reduction in pulmonary ventilation (fig. 6). Four patients became completely apnoeic for periods of up to fourteen minutes, six others required augmented respiration.

A further fifteen patients who were to be relaxed by a 0.1 per cent solution of suxamethonium chloride were each given 10 mg gallamine shortly after their drip infusions had been started. In four of them little effect could be seen; in seven, there was a definite increase in pulmonary ventilation (fig. 7a), and in the remaining four, a slight reduction for three or four breaths was followed by a small but definite increase (fig. 8a). It was thought that these uneven results were related to

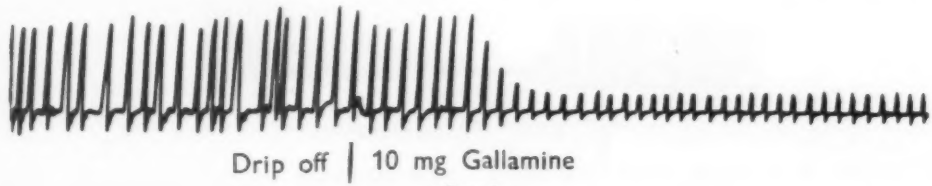

FIG. 6
Effect of 10 mg gallamine on patient who had been on suxamethonium chloride drip for 1 hour.

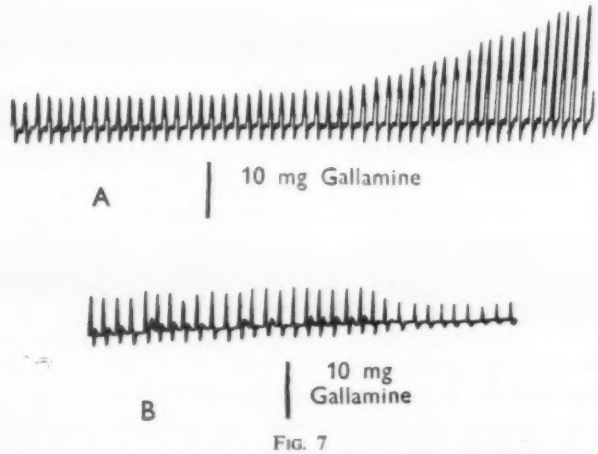

FIG. 7
Effect of 10 mg gallamine on patient on suxamethonium chloride infusion.
A. Soon after infusion was started. B. At end of operation.

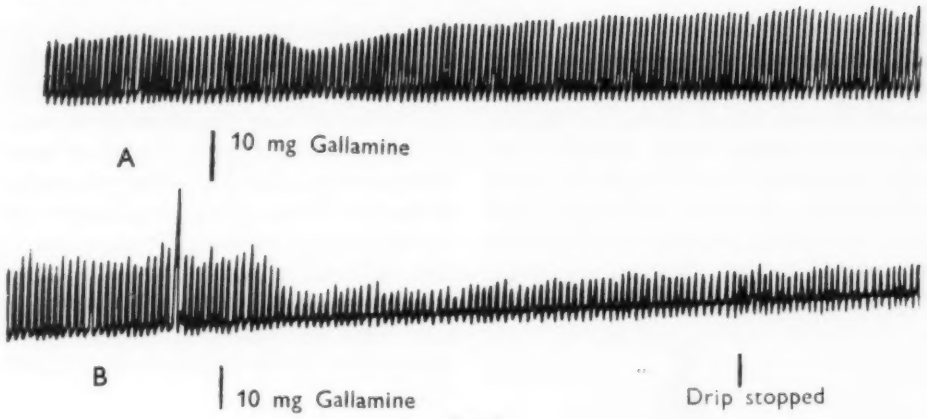

FIG. 8

Effect of 10 mg gallamine on another patient on suxamethonium chloride infusion.
A. Soon after infusion was started. B. At end of operation.

the varying amounts of suxamethonium chloride the patients had received when the gallamine was administered. Post-operatively each of these fifteen patients was again given 10 mg gallamine, and, like the twenty-two mentioned previously, all showed a definite reduction in pulmonary ventilation (fig. 7b, fig. 8b), one became apnoeic and two others required aided respiration.

In all, thirty-seven patients were each given 10 mg gallamine at the end of operations during which they had been relaxed by intravenous drip infusions of suxamethonium chloride. Five of them became apnoeic, eight others required artificial respiration, and all the remainder showed an immediate reduction of pulmonary ventilation of greater or lesser degree and duration.

These observations suggested that when a certain amount of suxamethonium chloride had been given to a patient over a certain period of time, the drug became more akin to a competitive blocker than to a depolarizer.

Succinylmonocholine.

It has been shown (Whittaker and Wijesundera, 1952; Lehmann and Silk, 1953) that the normal breakdown product of suxamethonium chloride is succinylmonocholine which itself has weak myoneural blocking properties. The question which naturally arose was whether these rather surprising responses to neostigmine and gallamine were in fact due to interaction of these drugs with succinylmonocholine, and whether in man the latter drug was d-tubocurarine-like in action. Little clinical work has been done with succinylmonocholine. Ellis et al. (1953) had concluded that in animals this drug resembled a depolarizer more closely than it did d-tubocurarine types, although Foldes et al. (1954) who gave it to ten human subjects reported that none of them fasciculated. He found that doses of 5–7 mg per kg of succinylmonocholine caused myoneural blocking which came on in 3–5 minutes, and lasted 8–12 minutes, but did not cause respiratory depression. Clinical trials of succinylmono-

choline were carried out and confirmed that its length of action was considerably greater than that of suxamethonium chloride. It was found, however, that the drug acted much more rapidly than Foldes suggested, and though no actual fasciculation was seen, its initial result was a very definite stimulation. This rapid response and marked effect on respiration are shown clearly in figure 9.

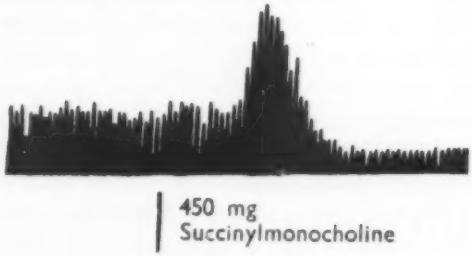

FIG. 9

Effect of 450 mg succinylmonocholine on patient weighing 70 kg, showing speed of onset, initial stimulation and respiratory depression.

After these preliminary trials, thirteen adult patients premedicated with papaveretum 20 mg, hyoscine 0.4 mg, were induced with 400–500 mg thiopentone, intubated, maintained on nitrous oxide 6 litres, oxygen 2 litres, "semi-open" method, and once they were settled were given succinylmonocholine until their respirations were definitely reduced. This was accomplished with doses varying from 9 to 11 mg per kg. Seven of them were then given 10 mg gallamine. In each case the pulmonary ventilation increased considerably, the gallamine having such an antagonistic action that the depression caused by the succinylmonocholine was virtually removed (fig. 10). The other six patients were each given 2 mg neostigmine preceded by 1 mg atropine. In each case this was followed by a slight increase in pulmonary ventilation (fig. 11), but it was only slight and was very different from the restoration which followed 10 mg gallamine.

These reactions showed that in man as well as in animals succinylmonocholine, at least initially, is predominantly a depolarizing agent. Gray (1956) suggested the possibility that this drug might itself possess a dual action. Seven patients were therefore premedicated with papaveretum 20 mg, hyoscine 0.4 mg, induced with 400 to 500 mg thiopentone followed by 500 mg succinylmonocholine, and, after intubation were maintained as before on nitrous oxide and oxygen. They then received a further 1,000 to 1,700 mg of succinylmonocholine by drip infusion over the next 1 to 1¼ hours. Postoperatively six of them were given 10 mg gallamine, the drip infusions being continued. In each case the gallamine immediately caused a slight reduction in pulmonary ventilation which lasted ½ to 3 minutes but did not necessi-

FIG. 10

Effect of 10 mg gallamine on patients depressed with succinylmonocholine.

tate any augmentation of respiration (fig. 12). One mg of neostigmine preceded by 1 mg atropine then caused a definite increase in pulmonary ventilation (fig. 12). In the seventh patient, 1 mg atropine and 1 mg neostigmine without previous gallamine, similarly resulted in a reversal of the depression caused by succinylmonocholine. These observations supported the theory that succinylmonocholine itself has a dual action when given in very large doses. The amounts of succinylmonocholine given to the last series of patients, 1,500 to 2,250 mg, would be derived from roughly 2,000 to 3,000 mg of suxamethonium chloride, that is, far more than would normally be given clinically, and the dual action of this weak myoneural blocking agent is probably not very important. It is unlikely that it played more than a small part in the reaction to gallamine and neostigmine observed in patients who had received suxamethonium chloride by drip infusion.

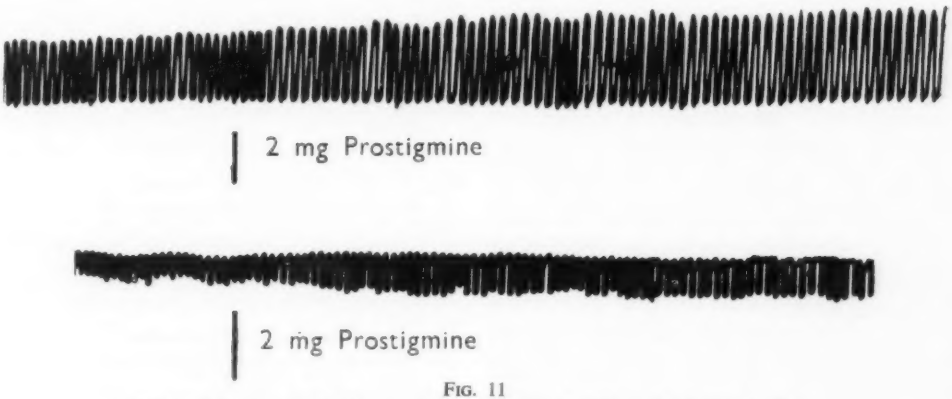

FIG. 11
Effect of 2 mg neostigmine on patients depressed with succinylmonocholine.

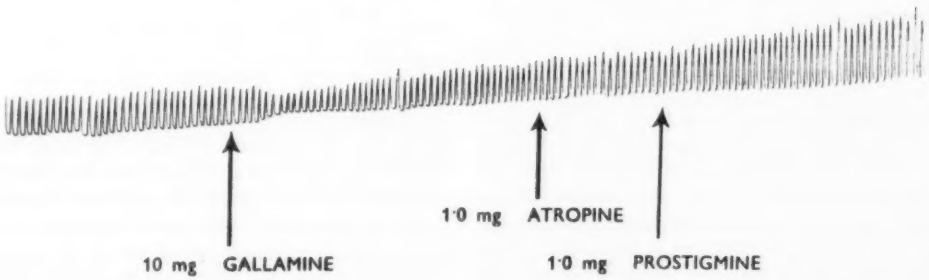

FIG. 12
Effect of 10 mg gallamine and later 1.0 mg neostigmine on patient who had received 1,950 mg succinylmonocholine over 65 minutes.

CONCLUSION

It is considered that the observations reported in this paper justify the conclusion that when a patient is given fairly large doses of suxamethonium chloride by drip infusion, this drug and possibly the succinylmonocholine formed as an interval product in its normal hydrolysis, change their mode of action and become antidepolarizing agents. While they in no way explain why very occasionally the effect of suxamethonium chloride should be unduly prolonged, they do suggest that if ever this condition is encountered an adequate dose of neostigmine should be administered.

SUMMARY

(1) A case is reported of prolonged apnoea after suxamethonium chloride in a patient with a normal serum cholinesterase, in whom the respiratory depression was increased by gallamine, but removed by neostigmine.

(2) Sixty-two patients who had received suxamethonium chloride by intravenous drip throughout operation were given either 2 mg neostigmine or 10 mg gallamine. Neostigmine usually had an antidotal effect, gallamine always caused potentiation.

(3) This effect of gallamine may have been partly due to interaction with succinylmonocholine which also has a "dual" action when given in very large amounts.

(4) Neostigmine has a definite place in the treatment of prolonged apnoea or reduced pulmonary ventilation due to suxamethonium chloride.

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BOOK REVIEW

Local Analgesia: Head and Neck. By Sir Robert Macintosh and Miss Mary Ostlere. Published by E. and S. Livingstone Ltd. Price 27*s.* 6*d.*

Sir Robert Macintosh is a past master in the art of getting expert collaborators to assist him in the numerous books for which he is responsible. This one is the latest in the series which began with his book on lumbar puncture and conforms to the high standard set by that volume. Teaching by pictures has become very popular of late and it is clear from the number and excellence of the illustrations that the authors are enthusiastic believers in this pleasant method. The book itself will not only be of great help to those who practise local analgesia but may be the means of discovering the obscure origin of a referred pain. 27*s.* 6*d.* is the highest price of any of the books in this series but it is a pleasure to handle and possess a volume so beautifully printed and illustrated—the first step to the possession of all the knowledge contained therein.

E. Falkner Hill

Brit. J. Anaesth. (1956), **28**, 169

TWO MORE RESPIRATORS

BY

J. A. G. HORTON, J. S. INKSTER AND E. A. PASK

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BOTH of these respirators are of the intermittent positive pressure type and in both the lungs are inflated to a predetermined pressure which may be adjusted between 6 and 40 mm Hg. The inflation then cuts off and expiration is allowed.

Provided that a suitable source of gas for inflation is used, the respirators allow the lungs to be inflated quickly, at flow-rates faster than 60 litres per minute, so the phase of positive pressure inflation can be very brief and most of the time cycle can be given to expiration and pause. Thus, mean intrathoracic pressure can be kept low. When the predetermined cut-off pressure is reached, the circuit is abruptly opened to the atmosphere so that expiration starts promptly. When the respirator is operated in the intermittent positive pressure mode, the residual pressure is negligible—less than 0.20 cm H_2O.

When a suitable source of suction is available, either respirator can control it and permit negative pressure to be applied to the lungs during expiration. Suitable sources of suction are vacuum cleaners, oxygen injector devices, etc. Both respirators operate from low pressure sources of gas or air at pressures between 30 and 70 mm Hg. Both of the respirators are entirely pneumatically operated and both are reasonably "economical". The flow of gases is cut off and conserved during expiration and pause, and the amount of gases needed to operate the mechanisms is small. For this reason, and because of the low pressure source, either respirator can be operated by the flow of gases from a continuous flow anaesthetic machine using non-rebreathing technique. For this technique the gases are stored in a large reservoir, such as a 2-gallon reservoir bag in a restraining net. A pressure relief device such as a water seal is provided.

Of course, the respirators will operate from other sources of air or gas, such as vacuum cleaner blowers, air entraining injectors, and so forth. Instead of directly inflating a patient's lungs, they can be caused to create pressure in a hollow vessel in which is contained a breathing bag, so that the breathing bag is intermittently compressed. In this case the patient's lungs can be inflated from a secondary rebreathing closed circuit.

The rate of inflow during inflation can be controlled, if for any reason this is desired. The pause after the completion of an inflation until the beginning of the next can be controlled without affecting the speed of inflation, so that repetition rate is continuously variable over the range 4–50 per minute.

By the addition of a "triggering" valve,

either respirator can be made sensitive to a patient's respiratory attempts. In this mode of operation, whenever the patient creates a negative pressure in the airway of 1.5 cm H_2O, the machine inflates the lungs to a predetermined pressure and then cuts off. A basic automatic rhythm can, if desired, be superimposed on this patient sensitive operation.

The first respirator is shown diagrammatically in figure 1. Its main components are:

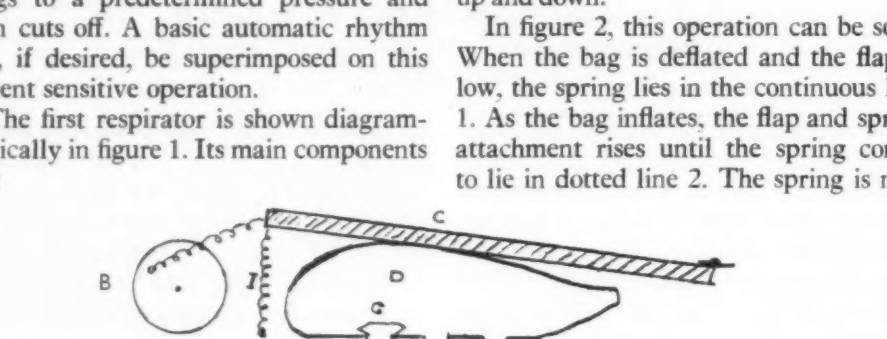

FIG. 1

(1) A rotary tap 'A' which controls the inspiratory and expiratory flow. It consists of a Tufnol core in a brass sleeve and its bores are at about 80° to one another. The core is mounted on ball bearings and rotates freely. In use, it oscillates through 80°, so that alternatively the inspiratory and expiratory channels are open. The oscillation of the tap is controlled by

(2) A toggle mechanism seen also in figure 2. The Tufnol core of the tap is attached to a wheel 'B' on which there is a peg. To the peg is attached a light coiled tension spring. The other end of this spring is attached to the end of a hinged flap 'C' which rests upon an anaesthetic breathing bag 'D'. In operation, this bag inflates and deflates and thus carries the flap up and down. The end of the tension spring attached to the flap is also carried up and down.

In figure 2, this operation can be seen. When the bag is deflated and the flap is low, the spring lies in the continuous line 1. As the bag inflates, the flap and spring attachment rises until the spring comes to lie in dotted line 2. The spring is now above the centre of the wheel and the system is unstable. Therefore, the wheel suddenly "flips" round so that the spring comes to lie in the continuous line 3. The rotating tap changes, the inspiratory

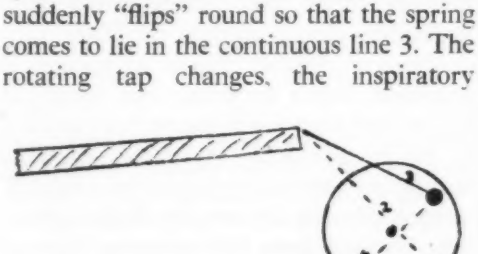

FIG. 2

channel closes and the expiratory channel opens. The patient's lungs deflate immediately, and later the control bag 'D' does so also. As this occurs, the flap falls and eventually the spring comes to lie in position 4, which again is unstable, so that again the wheel and tap "flip" round to bring the spring into position 1, and the cycle starts again, the inflation channel now being open. The operation of the machine can now be followed from figure 1. The machine is shown with the bag 'D' inflated and the flap 'C' in its upper position. The wheel 'B' has rotated so that the inlet channel is closed and the outlet channel of the tap is open. If the reader will imagine that the bag 'D' deflates, the flap falls and the wheel and tap rotate to the alternative position, the outlet channel will be closed and the inlet channel open. In this state, the gases flow in from the source and pass through the tube 'E' to the patient and also to the bag 'D'. The gases cannot escape, since we imagine the outlet channel to be closed. Thus the patient's lungs and the bag 'D' become inflated together. Air *flows into* the bag 'D' through the tube 'F' which has a nonreturn valve 'G' and also to a lesser extent through tube 'H', which has a variable constriction (tap or screw clip). When the patient's lungs are inflated to the desired pressure, the bag 'D' becomes distended and the flap 'C' rises to its upper position. At this point, the wheel 'B' "flips" into its alternate position and carries the tap with it. The inlet closes, the outlet opens and the patient's lungs deflate immediately. The bag 'D' cannot deflate immediately, for the nonreturn valve 'G' prevents the escape of air through the tube 'F' and all the air in the bag must *escape* through 'H'. If 'H' be constricted, the bag deflates slowly and until it is fully deflated, the outlet port remains open and the inlet closed. Thus, by varying the constriction in 'H', the pause between respirations is controlled.

During the inspiration phase, inflation of the lungs and the bag 'D' continues until enough pressure develops to force the flap 'C' into its upper position. Anything which hinders 'C' from rising will therefore cause the patient's lungs to be inflated to a higher pressure. This is the function of the adjustable spring 'I'. It controls the inflation pressure at which cut-off of inflow, and opening of the outlet occurs.

Because the tap 'A' positively controls inlet and outlet, it follows that:

(*a*) Suction (regulated by a gravity controlled valve) can be applied to the outlet to create a negative pressure in the lungs during the expiratory phase.

(*b*) The inflowing gases are conserved during the expiratory phase and because of this "economy" the use of anaesthetic gases without rebreathing becomes practicable.

The Patient-triggering Device.

If the reader will imagine that inflation of the lungs has just been completed and the bag 'D' is in the state shown in the diagram so that it is deflating (but slowly because of the restriction in tube 'H') he will realize that if a means could be found of opening a large hole into the bag 'D', it would immediately deflate and a new inspiration would be started.

To this end, the outlets 'J' and 'K' (shown closed by bungs in figure 1) are

connected by tubes to the similarly marked tubes on the magnetic patient-trigger valve shown in figure 3. A sensitive nonreturn valve 'L' (fig. 1) is put into the outflow tube.

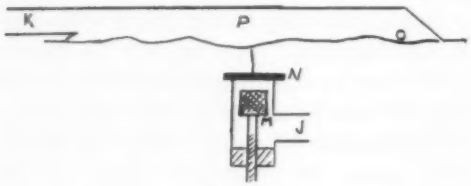

FIG. 3

The outlet 'J' is still effectively closed, for (fig. 3) its outlet to the air is sealed by a rubberfaced iron disc 'N', held down by the magnet 'M'. This magnet exerts sufficient pull to keep the disc 'N' in place against all working pressure in the bag 'D'. The disc 'N' is, however, also attached to a large slack diaphragm 'O' which forms one wall of a shallow chamber which is, of course, in communication with the outflow tube (fig. 1) through 'K'. If, during the period allowed for exhalation or pause, the patient makes a feeble attempt to breathe, the nonreturn valve 'L' closes and a small suction is created in the chamber 'P'. This suction acting over the large area of the diaphragm 'O', suffices to lift the disc 'N'. 'J' now forms a wide-open exit for the gases from the bag 'D' (fig. 1). The bag promptly deflates and in consequence the tap 'A' turns and an inflation starts.

The construction of the respirator can vary. Figure 4 shows the arrangement we have used so that the device can be mounted on the bottom shelf of a Boyle's machine. The patient-triggering valve is on top of the respirator. Figure 5 shows the construction of the tap-operating spring toggle, as we have made it.

This machine has proven useful in the operating room where its quiet operation, compact construction and freedom from electrical connections are convenient. We have also successfully used it on two cases of prolonged respiratory paralysis—one of seven and one of four weeks duration. One of these patients, who suffered from myasthenia gravis, had for most of the time feeble and quite inadequate respiratory power. This sufficed, however, to "trigger" the respirator so that the degree of ventilation remained under the control of the patient's own physiological regulating mechanisms, though the machine supplied the effort. This seemed to us

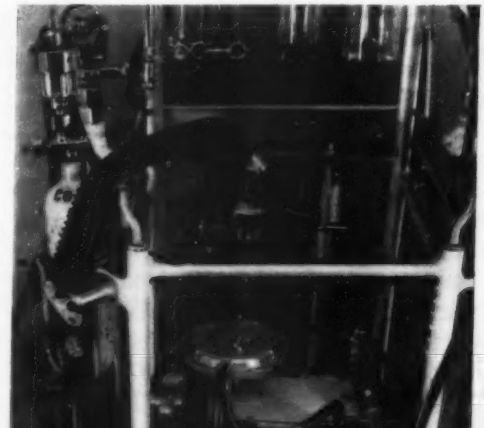

FIG. 4

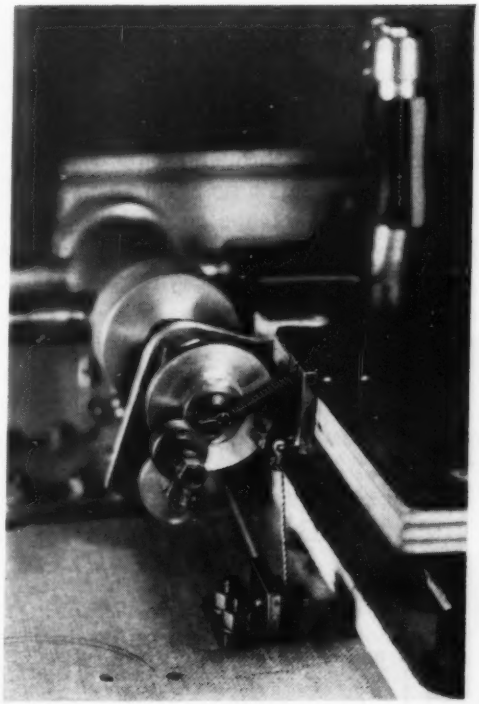

FIG. 5

very helpful, as one had no worries concerning excess or deficit of carbon dioxide.

The second respirator operates on similar principles but is easier to construct and a good deal smaller. It has up to now been used only for 50 cases in the operating room, under constant supervision. In these conditions it has given no trouble, but we cannot yet claim to have substantial experience of its reliability. The essential parts are contained within the outer tube 'A' (fig. 7) with its perforated partitions 'B' and 'C', and an unperforated partition 'D'. Through these partitions there passes the valve rod 'E' which makes a nice freely sliding fit. The rod bears the valve discs 'F' and 'G'. They are rubber faced and the disc 'F' is of iron and comes under the influence of the magnet 'H'.

With this preliminary, the action of the respirator can be explained.

The respiratory gases enter at 'I' from the reservoir, past the valve disc 'F' and through the partition 'C' and out through the tube 'J' to the patient. The patient's lungs are inflated and as the pressure in them rises, so it must also rise in the tube 'K' and the chamber 'L', for the valve disc 'G' is down and seals the perforation in the partition 'B'. Pressure also rises in the concertina bellows, since gas passes into it through tubes 'N' and 'O'. The concertina rises and draws up the rod 'P',

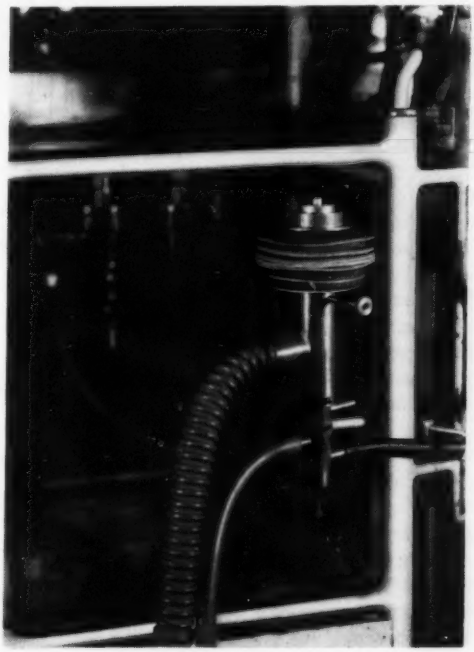

FIG. 6

so that soon the loose washer 'Q', resting upon the spring impinges upon the stirrup 'R', which is attached to the valve rod 'E'. This rod is pulled upon and suddenly the pull of the magnet upon the disc 'F' is overcome. The valve rod suddenly moves, so that the disc 'F' now seals the perforations in partition 'C' and the disc 'G' exposes those in 'B'. The reservoir pressure maintains the seal of the valve disc 'F'. The inflation pressure is cut off, and exhalation occurs freely through the partition 'B' and the outlet 'T'.

The concertina bellows now start to descend. The only escape for the gas contained in them is through the tube 'N', for the tube 'O' bears a nonreturn valve and the wider part of the rod 'P' has been drawn up and seals all channels in the plug 'U'. The tube 'N' may be constricted

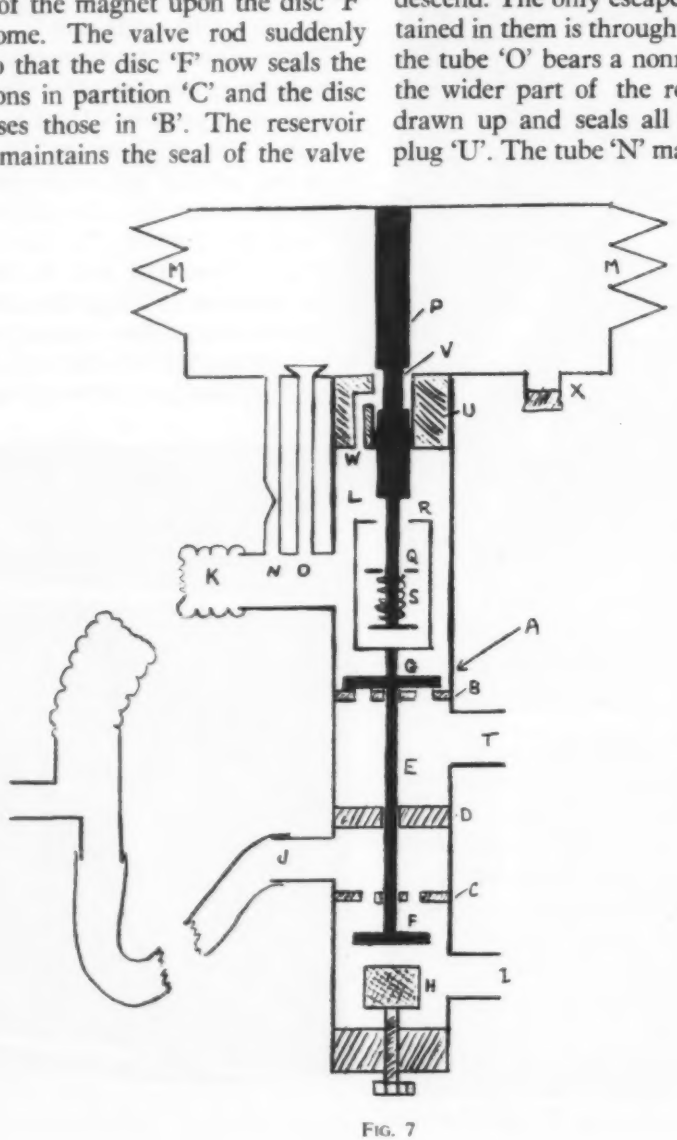

FIG. 7

to a variable degree so the descent of the bellows and, therefore, the pause before the next respiration can be controlled. Eventually, however, the narrowed portion 'V' of the rod 'P' allows the subsidiary channel 'W' in the plug 'U' to open. This provides a large leak of air from the bellows 'M', so that 'M' completes its descent quickly. The lower end of the rod 'P' impinges on the top of 'E'. The disc 'F' is thus displaced from its partition 'C' and the pressure difference across it is broken. It comes immediately under the influence of the magnet 'H' and is drawn abruptly downward. Thus the cycle is complete and a new inflation of the lungs begins. The pressure of inflation is controlled by placing weight discs on top of the concertina bellows, which hinder their distension and thus increase the pressure needed to elevate them to the change-over position. Figure 6 shows the device in use upon a Boyle's machine.

This respirator can also control negative pressure and can be made " patient-triggered" by connecting to the tube 'X' a patient-triggering valve similar to that already described, but somewhat smaller in size.

ACKNOWLEDGMENT

We wish to acknowledge the great assistance which we have received from Mr. N. Burn, Senior Technician in the Department of Anaesthetics.

BOOK REVIEW

Anesthesia in Ophthalmology. By Walter S. Atkinson, M.D., Associate Clinical Professor of Ophthalmology, New York University, Postgraduate Medical School. Published by Charles C. Thomas, Springfield, Illinois, U.S.A. Pp. 99; 44 illustrations.

This little book is written by an ophthalmologist for his own colleagues. It is natural therefore that methods of local analgesia should predominate. From the title, however, one expects a review of all methods of anaesthesia for this field of surgery, and in this the reader may be disappointed. Dr. Atkinson refers scornfully and in an idiom happily no longer current in Europe to the " less stoical races." He nevertheless devotes 20 pages to the problems of pre-operative sedation, indicated, as he puts it himself, only for " more excitable races, neurotic, and mentally disturbed patients." Then come 30 well illustrated pages devoted to the now more or less standard techniques of local analgesia for ophthalmic operations. This is followed by no less than 14 pages on the treatment of emergencies, taken largely from Cullen's excellent monograph on the subject and illustrated by the humorous cartoons from that book. In spite of the fact that room is found for a whole page illustration of what must be an incomprehensible apparatus for oxygen insufflation, and another whole page illustration showing ten different airways, it is disappointing to find the whole of general anaesthesia treated in some 6 or 7 pages. The author feels it is the duty of ophthalmologists " to be sufficiently familiar with different types of general anaesthesia " so that they can " intelligently confer " with anaesthetists on the selection of method. This commendable aim is unlikely to be realized by perusal of the miscellany of information given. In these few pages the ophthalmologist will find helpful facts, such as that the blood sugar level during the administration of ethyl ether " may be elevated as much as 100 per cent to 200 per cent ", that " pentothal sodium is compatible with most anaesthetic agents and also with curare ", and that an endotracheal tube minimizes explosion when ether is administered because " after the first few breaths the humidity is raised so that there is little danger from static spark in the system". The book contains many points of " know-how " in connection with regional analgesia for this branch of surgery. It summarizes Dr. Atkinson's outlook on and practice of analgesia for ophthalmic surgery. It is far from being a survey, by any standard, of the scope of general anaesthesia in this field.

William W. Mushin

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THE FAZAKERLEY RESPIRATOR

BY

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INTRODUCTION

"In breathing there are two kinds of blessings: inhaling the air and exhaling it; the former is oppressive, the latter refreshing, so strangely is Life mingled. Thank God when He lays a burden on thee and thank Him when He takes it off."—GOETHE.

IT is a daily event in anaesthesia, and not uncommon in other spheres of medical practice, to meet with the patient who is in need of relief from the burden of inhaling; and one means of relieving such a patient of his burden is the application of positive pressure ventilation.*

The safe application of positive pressure ventilation is, however, no easy matter: for much time, thought, and energy, must be expended if the disadvantages of the method are to be surmounted. If they cannot be surmounted—and the problems they give rise to increase in difficulty as the period of ventilation lengthens—complications develop, and, in the long term medical case, it is then very soon apparent that the resort to positive pressure ventilation has failed: that it has resulted in the conversion of what should have been a rapidly fatal condition into a lingering and exceptionally distressing terminal illness.

One of the disadvantages of positive pressure ventilation is that the method is not only incapable of assisting the patient in exhaling but also capable of causing exhalation to be prolonged: for it is practicable only when the diaphragm and the muscles of the chest wall are atonic; and when these muscles are atonic the lungs are apt to deflate slowly, particularly if they are fibrotic or oedematous or if the chest wall has lost its natural resilience. Now if exhalation is unduly prolonged the patient may still be exhaling at the time the inflation pressure is applied; and in that event exhalation will be cut short, and the resting volume of the lungs will increase.

This increase can produce complications in the circulatory, respiratory, and muscular systems. It may raise the mean intrapleural pressure and so impede the venous return to the heart. It will bring about an increase in the volume of the deadspace air and so impair the efficiency of ventilation. Moreover, by holding the chest partly expanded in the intervals between inflations, it will prevent the diaphragm and the muscles of the chest wall from regaining their normal resting lengths, and may thereby jeopardize the functional recovery of the internal intercostal muscles;

* In this paper the terms "positive" and "negative" are used to indicate whether a pressure should be added to or subtracted from the atmospheric pressure in order to obtain its absolute value. They are also used qualitatively, to indicate how a pressure with which one is dealing ranks in relation to the atmospheric pressure—a use which it is thought is justifiable on the grounds that the absolute value of a positive pressure must always be greater, and the absolute value of a negative pressure less, than the the atmospheric value.

for these muscles will be held under tension all the time that the chest is held expanded—and muscle which has been stretched whilst in the paralysed state either takes a long time to recover its tone or fails to recover it at all. Even the relatively short applications of positive pressure ventilation used in anaesthesia may, by their effect of continually relaxing the external intercostals and continually stretching the internal intercostals, result in the former muscles recovering their tone before the latter; a circumstance that would interfere with the concerted action of these muscles in the immediate post-operative period and delay the return of the patient's full expulsive powers.

Another disadvantage of positive pressure ventilation is that it subjects the chest to unidirectional stresses when the muscles are paralysed, be borne by the bone, cartilage and fibrous tissue, of the chest wall. These tissues are malleable or deformable; and it is because of that, and because the ventilating pressure, though a small enough force in itself, is applied to them at the rate of some 20,000 applications each 24 hours, that it is undesirable that the stress produced by the pressure should be unidirectional.

Just how long the chest can withstand the stresses of positive or negative, pressure ventilation (for the latter too produces unidirectional stress) is uncertain. It has, however, been the writer's experience that a " ballooning out " of the upper and anterior parts of the chest wall is often to be detected by the end of the third or the fourth week of ventilation—and that the appearance of the chest by the end of the third or the fourth month of ventilation is not infrequently such as would justify its being described as " blown ".

That the deformity appears first in the upper and anterior parts of the chest is probably because there the internal thrust of the intrathoracic pressure is assisted by the external pull of the accessory muscles of respiration. It always heralds the approach of a rapid deterioration in the effectiveness of the pulmonary exchange, and it should not, of course, be permitted to develop—but how it is to be prevented from developing is another question, and one that is likely to remain unanswered until the orthopaedic implications of artificial ventilation are better understood than they are today.

It is not improbable, however, that the structural changes produced by ventilation vary as the mean value of the ventilating pressure varies, and that they would be reduced to nil if the mean value of the ventilating pressure could be reduced to zero. But the mean value of the pressure cannot be reduced to zero when positive pressures are used alone: it can be so reduced only when two pressures of opposite sign are at work—when, for example, a positive inflation pressure alternates with a negative expiratory pressure. To put the matter in another way; an expansion strain requires for its correction a compression strain; and a negative expiratory pressure will create a compression strain by causing the chest to be compressed by the atmospheric pressure in the intervals between inflations. Another means of limiting the structural changes produced by ventilation would be to limit the expansion of the chest by the application of some form of support or " splint " to the chest wall.

To return for a moment to the source of some of these problems—namely, the prolongation of exhalation. That it is possible for exhalation to become dangerously prolonged follows from the fact that positive pressure ventilation plays no part in the production or in the control of pulmonary deflation; that it is a form of ventilation in which only one phase, usually less than one-half, of the ventilatory cycle is under the anaesthetist's full control.

And it was to provide the anaesthetist with a mean of controlling both inflation and exhalation, and of assisting the patient in exhaling, that the respirator shown in figure 1 was designed.

THE RESPIRATOR

This, the Fazakerley respirator, provides positive inflation pressures of 10 to 30 cm H_2O, and provides for the control of the frequency and the phases of the ventilatory cycle. And it can also be made to develop a negative pressure in the airway during the exhaling or expiratory phase.

For its motive power, the respirator depends on compressed air: the supply requirements being a flow of 20 to 30 litres a minute and a supply pressure of 100 to 360 mm Hg. In the absence of a suitable air supply, oxygen may be used, but in the interests of economy the gas is usually diluted with air before it is delivered to the machine, its admixture with air being readily effected by means of an air-entraining device that will be described later.

The principal parts of the respirator are "arrowed" in figure 1. They are: an intermittent positive pressure, or I.P.P., unit (3); an expiratory pressure control, or E.P.C., unit (2); a glass pressure bottle (1); a manometer (6); a corrugated flexible connecting tube (4); and an air lead (5).

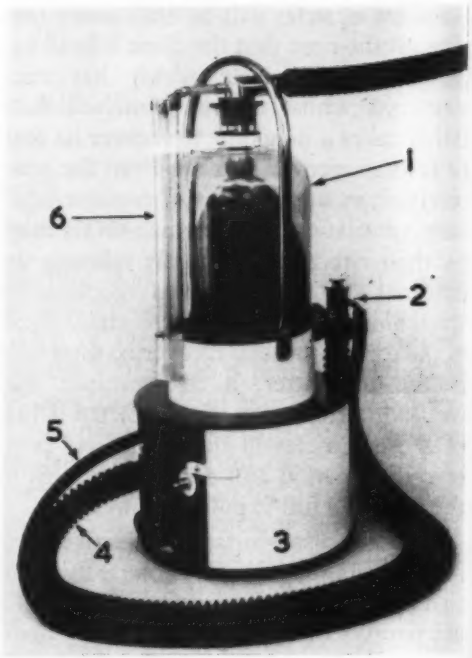

FIG. 1

Of these components, the I.P.P. and the E.P.C. units are those responsible for the production of the positive and the negative pressures. They also provide the innovatory features of the respirator, and each unit will therefore be described in detail.

Before they are described it must, however, first be explained how the machine works as a whole, although a short explanation is all that will be required, because the general principles on which the pressure-cycled type of respirator works are by now well known. Briefly then, the Fazakerley respirator operates as follows:

Inside the glass pressure bottle is a one-gallon rubber bag. This is connected with and employed as the rebreathing bag of the CO_2 absorption apparatus that happens to be in use, when compression and expansion of the bag will produce inflation and deflation of the patient's lungs. The necessary compression and expansion of the bag is brought about by alternately raising and lowering the air pressure in the bottle: the I.P.P. unit producing a positive pressure in the bottle, and the E.P.C. unit a negative pressure (or an atmospheric pressure), turn about. By generating and applying these pressures the respirator acts as a pneumatic hand and serves as a mechanical means of ventilating the lungs.

The I.P.P. Unit (fig. 2).

The air supplied to the respirator passes through the air-lead (A) to reach and enter the E.P.C. unit, which unit should, for the present, be regarded as a plain L-shaped connecting piece that has been fitted with a side-tube (S).

From the E.P.C. unit the air is free to flow through the corrugated connecting tube (E), the distributor tube (D), the short flexible connection (F), and the cylinder (C), to an exhaust port (e). It is also free to flow into the glass pressure bottle by way of the mount (M).

The port (e) is opened and closed by a mechanically operated valve (V), with the result that the air admitted to the apparatus is alternately able and unable to escape from the apparatus to the atmosphere; the period during which the port is open constituting the expiratory phase, and the period during which it is closed the inflation phase.

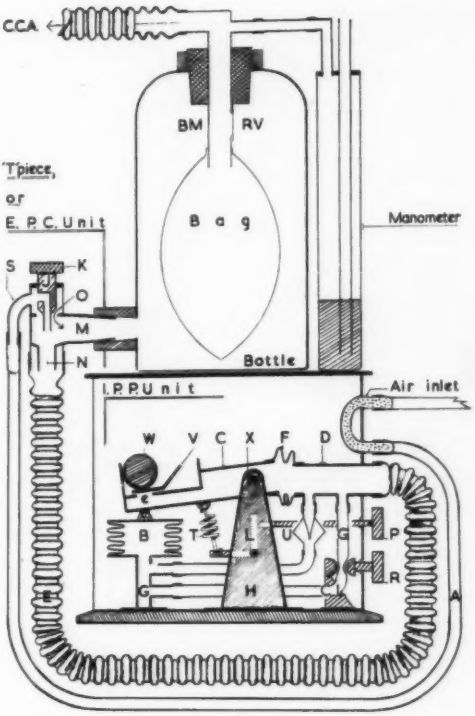

FIG. 2

The Inflation Phase of the Ventilatory Cycle (figs. 2, 3, 4).

When the exhaust port is closed, the air supplied to the respirator flows into a closed system. It therefore creates pressure.

This pressure is applied to the bag in the bottle and, through a one-way valve (U), to a bellows (B).

The bag in the bottle is compressed by the pressure and its contents are insufflated into the patient's lungs, which inflate.

The bellows too inflate in response to the pressure—but not until the pressure in the system is great enough to overcome the tension of a spring (T).

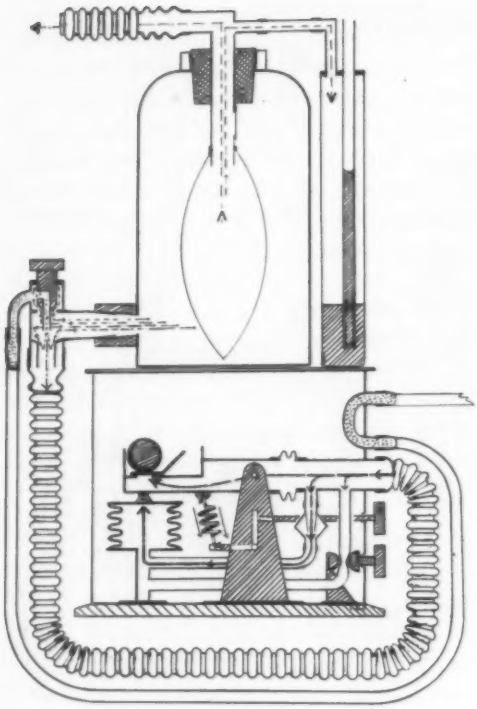

FIG. 3

This spring extends from the horizontal arm of a lever (L) to a hook located on the underside of the cylinder (C). Its action is to pull the lefthand end of the cylinder downwards against the bellows. The bellows therefore cannot expand until the expansion force of the air pressure inside them exceeds the compression force of the spring.

When the bellows do inflate, they drive the lefthand end of the cylinder upwards, causing the cylinder to tilt on the pivot (X) by means of which it is mounted on the brackets (H).

The slope of the cylinder is thus reversed, and the heavy ball (W) consequently rolls from the left- to the right-hand end of the angled perspex strip that forms the valve (V)—causing the valve to "see-saw" into a position which leaves open the port (e).

With the opening of the exhaust port the inflation phase ends and the expiratory phase begins, but before the expiratory phase is described the means by which the inflation pressure and the length of the inflation phase are controlled must be explained.

The Control of the Inflation Pressure (fig. 2).

The peak inflation pressure is the pressure present in the apparatus at the moment the exhaust port opens. It varies as the tension of the spring (T).

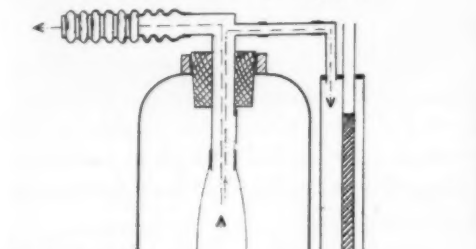

FIG. 4

To increase the tension of the spring, and so raise the inflation pressure, the anaesthetist turns the knob (P) clockwise. By doing so he screws a threaded rod to which the knob (P) is attached against the vertical arm of the lever (L), causing that arm of the lever to be pushed to the left and the horizontal arm of the lever to be depressed—when the spring will be further stretched and its tension increased. To lower the inflation pressure the anaesthetist turns the knob anticlockwise.

The Control of the Length of the Inflation Phase.

The length of the inflation phase varies as, and is controlled by varying, the rate at which air is supplied to the respirator.

The Expiratory Phase and its Control (figs. 5 and 6).

The opening of the exhaust port has the immediate effect of reversing the pressure gradient across the oneway valve (U), and the valve therefore closes. It also has the effect of dispersing the pressure in the bottle, so that the patient's lungs are free to deflate.

The bellows, too, deflate, but to do so they must expel the air they contain through the rubber tube (G), since this tube is the only exit from the bellows. The tube is furnished with a clamp (CL), which the anaesthetist can open and close by turning the knob (R) anticlockwise and clockwise respectively, and the rate at which the bellows deflate depends on the extent to which the clamp obstructs its lumen.

Now the more rapidly that the bellows deflate, the more rapidly will the spring (T) draw the lefthand end of the cylinder downwards again, the sooner will the cylinder regain its original angle of slope, and the sooner will the ball (W) roll back to close the valve and bring the expiratory phase to an end. Contrariwise, the more slowly that the bellows deflate the longer will be the period that elapses before the expiratory phase ends.

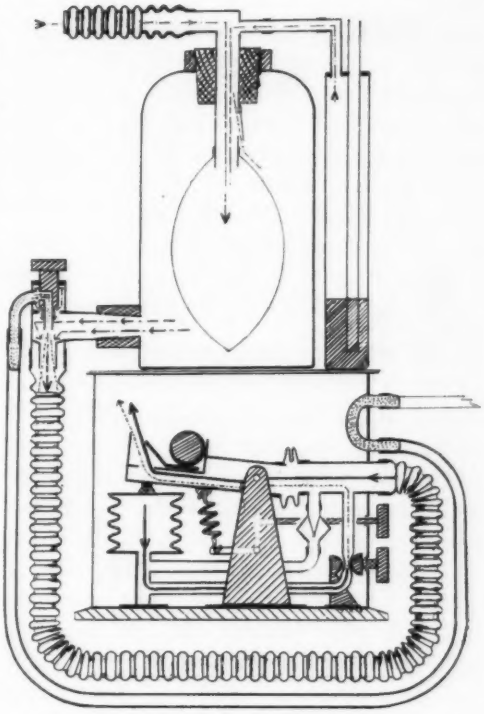

FIG. 5

The knob (R) therefore controls the length of the expiratory phase of the cycle: to provide an expiratory pause, the anaesthetist has only to turn the knob clockwise until the bellows deflate more slowly than the lungs deflate.

The Control of the Ventilatory Rate.

The ventilatory rate (or the frequency of the mechanical cycle) is governed by

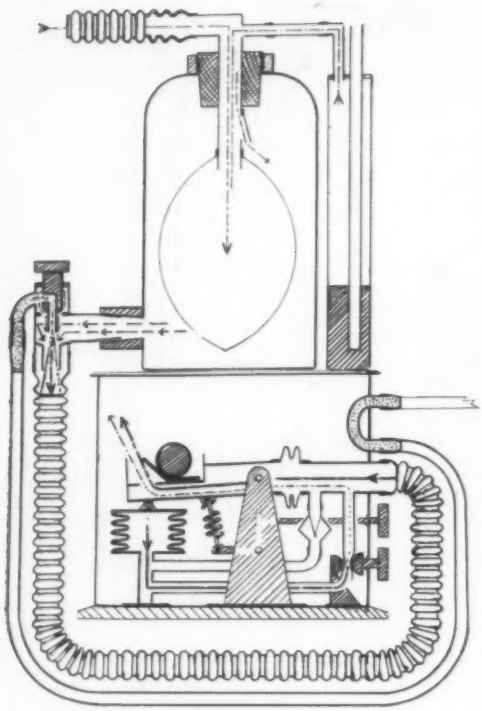

FIG. 6

the factors shown in the following equation:

$$\text{Rate} = \frac{60}{\text{Length of inflation phase in seconds} + \text{Length of expiratory phase, including any pause, in seconds}} \text{ cycles/min.}$$

Anything that reduces the value of the denominator of the equation will increase the rate, and anything that increases the denominator of the equation will reduce the rate. In practice, the anaesthetist usually alters the rate by providing a slightly longer or shorter expiratory phase.

The E.P.C. Unit (fig. 2).

The upper one-third of the E.P.C. unit forms a small air chamber. This chamber has an inlet for the admission of air, the side tube (S), and two exits for its discharge: the annular space (O), and the bore of the jet (J).

The first of these exits, the annular space, is a variable aperture, since clockwise rotation of the knob (K) will drive the cone-shaped point of the jet into the annular space, causing the space to close; whilst anticlockwise rotation of the knob will withdraw the jet, causing the space to enlarge.

The second exit, the bore of the jet is a fixed aperture.

Of the compressed air admitted to the air chamber, some will be discharged from the chamber by way of the bore of the jet valve, and some by way of the annular space; and the way in which the discharge of air is distributed between these two exits determines the pressure in the mount (M). For the air that is discharged from the chamber by the bore of the jet valve is injected into a venturi tube (N), and its entry into the venturi tube will tend to create a negative pressure in the mount; whereas the air that is discharged from the chamber by way of the annular space will enter the mount itself, under pressure—a circumstance that tends to create a positive pressure in the mount.

The two tendencies vary in strength as the airflows by which they are produced vary in strength; and since the anaesthetist can, by manipulating the knob (K), increase the strength of either flow, it follows that he can accentuate either tendency, and so produce a positive or a negative pressure in the mount at will. And that he can produce a positive or a negative expiratory pressure—because the pressure produced in the mount will be

propagated to the pressure bottle and reproduced in the rebreathing bag during the expiratory phase. During the inflation phase, the small pressure produced in the mount by the tendencies under discussion is overwhelmed to insignificance by the inflation pressure.

How the anaesthetist adjusts the expiratory pressure in practice is explained below.

To produce a negative expiratory pressure.

The anaesthetist turns the knob (K) clockwise in order to reduce the patency of the annular space and so increase its flow resistance. Once the flow resistance of the space exceeds the flow resistance of the bore of the jet valve, most of the air admitted to the air chamber will leave the chamber by the bore of the valve (i.e. by the easier route), with the result that more air will pass through the venturi tube than will pass into the mount. The dominant tendency will, therefore, be that produced by the venturi tube, and the pressure in the mount will become negative—and increasingly so as the knob continues to be turned. Once the space has been completely closed, no air at all can enter the mount and, the venturi effect being unopposed, the pressure in the mount may fall to as low as minus 10 cm H_2O.

To produce a positive expiratory pressure.

The anaesthetist turns the knob (K) anticlockwise in order to increase the patency of the annular space, and so reduce its flow resistance. Once the flow resistance of the space has fallen below that of the bore of the jet valve, most of the air admitted to the air chamber will leave by way of the annular space. More air will therefore pass into the mount than will pass into the venturi tube and the dominant tendency will be that produced by the expansion of air in the mount. The pressure in the mount accordingly becomes positive. Once the space is fully open, little or no air enters the venturi tube and, the expansion effect of the air entering the mount being unopposed, the pressure in the mount rises to around 5 cm H_2O.

To produce atmospheric expiratory pressure.

The anaesthetist turns the knob (K) one way or the other until the manometer registers atmospheric pressure during the expiratory phase. He will then in effect have matched the flow resistance of the annular space with that of the bore of the jet valve; and equal volumes of air will be passing into the venturi tube and the mount to produce equal but opposite effects.

From the point of view of clinical usage, the E.P.C. unit may be said to function only during the expiratory phase of the cycle. The pressure created in the mount by the interaction of the two forces just described does, however, play a minor role during the inflation phase of the cycle. A negative pressure, for example, then acts as an anti-inflationary force; as is evident by the rise in the peak inflation pressure that occurs when a negative pressure is cancelled, and by the fall in the inflation pressure that occurs when the strength of a negative pressure is increased. Conversely, the provision of a positive expiratory pressure raises, and its cancellation lowers, the peak inflation pressure. These side effects to the use of the E.P.C. unit have one, apparently quite unimportant,

result: that the *difference* between the maximum and the minimum pressure remains constant for any given setting of the inflation pressure control knob (P) no matter how the expiratory pressure control knob (K) may be set and reset.

MANOMETER; PRESSURE RELEASE VALVE; AIR-ENTRAINING DEVICE

There remain to be described: the manometer (fig. 2); the pressure release valve (fig. 2 (RV)); and the air entraining device.

The manometer is connected with the breathing circuit. Because of that, and because it is a water manometer, it serves not only as a pressure indicator but as a safety valve as well, for the height and the depth of the manometer tube will limit the positive and the negative pressures that the machine can apply to the lungs.

The pressure release valve (RV) consists of a rubber flap covering a hole in the bag mount (BM). The valve lifts to allow excess gas to pass from the breathing circuit to the bottle, and thence to the atmosphere during the expiratory phase. It prevents the rebreathing bag from overdistending during use.

The air-entraining device which is not illustrated here saves oxygen when the respirator is worked from a cylinder. Designed to be connected with B.O.C. oxygen valve MS.55, or MS.56, by a short length of stout-walled rubber tubing, and with the respirator by not more than 10 feet of ⅜-inch bore tubing, the device utilizes the injector principle to convert a small volume of oxygen at a high pressure into a larger volume of air and oxygen at a relatively low pressure. It is capable of supplying up to 40 litres of air-oxygen mixture a minute and of delivering the mixture, which contains 30 to 35 per cent oxygen, under a pressure of about 100 mm Hg. With the device in use 100 cubic feet of oxygen will run the respirator for from 6 to 8 hours, according to the depth and the frequency of the ventilation provided.

Here it would be as well to point out that the respirator is subject to the law of supply and demand, and that the more work that it is called upon to perform, the more energy in the form of air does it need to be provided with. The correct flow is always that which provides satisfactory ventilation and the type of inflation phase (rapid or slow) that the anaesthetist favours.

DIRECT INFLATION OF LUNGS

The lengths of the tubes joining the E.P.C. unit with the I.P.P. unit make the respirator cumbersome and detract from its appearance, but their lengths are a convenience when it is necessary to ventilate a patient with air or with an air-oxygen mixture in an emergency. For the respirator to be used in this way, the E.P.C. unit is detached from the pressure-bottle and connected to the endotracheal or facemask connection: and the long tubes enable this to be done with the minimum of delay.

CONCLUSION AND APPARATUS FOR STUDIES OF VENTILATION

In conclusion, this respirator was designed in the hope that the provision of a negative phase would enable some of the complications of positive pressure ventilation to be avoided, but it is emphasized that as yet there is only the most tenuous

evidence that the use of negative expiratory pressures is in any way protective. It should also be mentioned that the findings of a recent investigation suggest that there are occasions when the use of negative expiratory pressures is undesirable—during anaesthesia for *intra*thoracic procedures for example, when their use may lead to collapse of the contralateral lung, to underventilation with retention of CO_2, and a dangerous reduction in the uptake of oxygen.

In the course of this investigation it became necessary (i) to obtain serial samples of the air present in the trachea during expiration, and (ii) to record the mean ventilating pressure. To this end, two pieces of apparatus suitable for use in conjunction with the respirator were designed. Each is briefly described below.

Apparatus for the Continual Withdrawal of Samples of the Tracheal Air

Figure 7 shows the respirator connected with a simple absorption system, in which the volume of the exhaled air may be measured by a meter placed in the expiratory side of the circuit, and in which the fresh anaesthetic gases are admitted at a point that precludes their passing through the meter during the expiratory phase.

The rest of the apparatus is concerned with the withdrawal of air from the region of the tracheal bifurcation during, and only during, the expiratory phase, and with the delivery of the air withdrawn to a collecting bag attached at (S).

(M) and (N) are two bellows linked in such a manner that the expansion of one bellows will result in the compression of the other.

The lefthand bellows (M) are connected with the pressure bottle (P) of the respirator. The righthand bellows (N) are connected with the outlet (S), and with a tube (St) to which is attached a catheter whose tip lies near to the tracheal bifurcation.

During the expiratory phase, the bellows (M) are emptied by the suction then present in the pressure bottle, or (if it is not intended to use a negative expiratory pressure) by means of weights placed on top of the bellows. As the bellows (M) empty, so the bellows (N) expand. And as the bellows expand they fill with air drawn from the trachea.

During the inflation phase, the positive pressure in the pressure bottle expands the bellows (M) and as they expand they compress the bellows (N), driving the tracheal air contained in the latter towards and into the collecting bag attached at (S). Nonreturn valves incorporated in the bellows (N) maintain the necessary unidirectional flow.

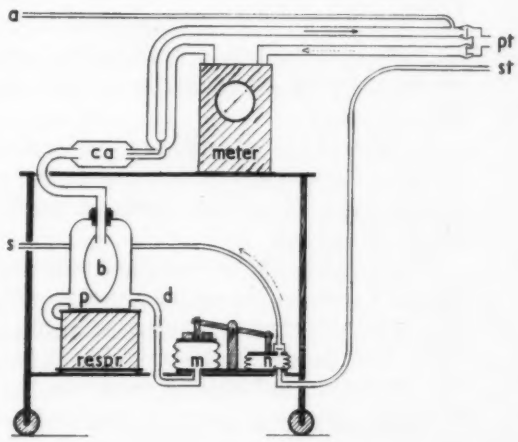

FIG. 7

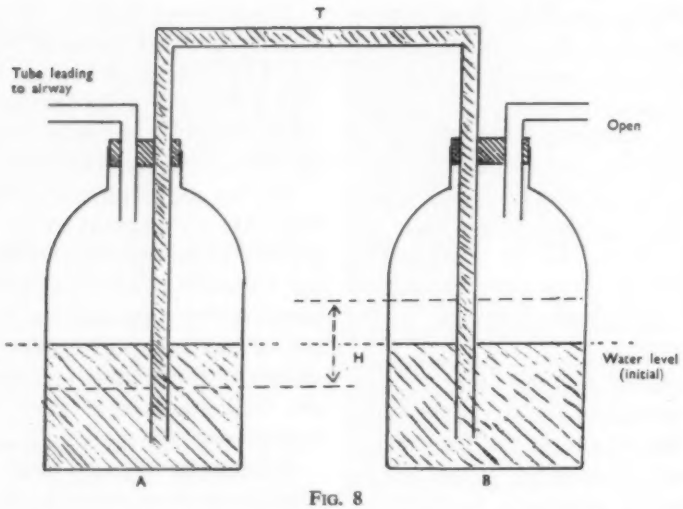

FIG. 8

A tube leading to an infrared gas analyser is substituted for the collecting bag when a breath-by-breath analysis of the exhaled air is required.

The Mean Pressure Manometer

The following method of measuring the mean ventilating pressure is based on the fact that the mean or average pressure in a system is the effective working pressure or the pressure continuously at work in that system.

In figure 8 (A) and (B) are two bottles of large capacity joined together by a syphon tube (T). Each bottle is partly filled with water.

When bottle (A) is connected with the patient's airway, the mean pressure will, if it is greater than zero, work to displace water from bottle (A) to bottle (B). At first the water level in bottle (B) rises steadily; but very shortly it ceases to rise and remains at a constant height above the water level in bottle (A). The difference in height (H) is the height of the water column that the pressure in the airway can sustain continuously: it is therefore the mean ventilating pressure, or a close approximation to that pressure.

The water levels alter when the mean pressure alters, but they do not oscillate (to any great extent) in response to fluctuation of the inflation pressure. This is because the arrangement allows of the displacement of a large volume of water over a period of minutes, but does not allow of the displacement of more than a few cubic centimetres of water during the second or so that each pressure-phase lasts.

ACKNOWLEDGMENTS

I am glad to have this opportunity of thanking Dr. H. J. V. Morton for his encouragement and helpful suggestions; thanking Dr. A. B. Christie, Mr. Ronald Edwards, and Mr. Kenneth Waddington, for the interest they have shown in the use of the respirator; and of thanking all the other people who have, in one way and another, helped me to press on with the building of the machine and with the writing of this paper.

I also acknowledge the technical assistance I have received from Messrs Elliotts (Liverpool) Ltd., the manufacturers of the respirator. They could not have been more co-operative.

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HYALURONIDASE IN EPIDURAL ANALGESIA

BY

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EPIDURAL analgesia was first performed successfully in 1901 by Sicard and Cathelin using a caudal approach through the sacral hiatus. Attempts to locate the epidural space via the lumbar route were made by various workers such as Heile (1913) and Pagés (1921), who used only a sense of touch. Technical refinements have developed and using any one of a wide variety of aids, it is now possible to make a successful injection in a high proportion of cases.

ADVANTAGES OF EPIDURAL ANALGESIA

The advantages of epidural analgesia are considerable. Prolonged analgesia in the operative field, with its associated reflex relaxation, is preferable to a general anaesthetic with relaxants, because the respiration is left unimpaired. In the early postoperative phase, the patient has analgesia associated with a near normal tidal volume, thus enabling coughing and breathing exercises to be carried out painlessly within a few minutes of the end of the operation. This may be of great benefit to the patient with concurrent pulmonary disease. Furthermore, the residual analgesia enables the patient to be in full command of his faculties by the time pain from the wound appears. This makes a sharp contrast with the restless semi-conscious patient often seen after deep general anaesthesia.

As with spinal analgesia, it is possible to cause considerable hypotension. This may be used where it is indicated to reduce bleeding, or it may be prevented or abolished by the exhibition of either a vasoconstrictor or a sympathomimetic amine such as methylamphetamine. As a method of controlled hypotension, it is easy to maintain, requires no complicated technique such as is necessary with hypotensive drugs, and can be swiftly and easily reversed when necessary.

In its effect, epidural analgesia closely resembles spinal analgesia and indeed some believe its action to be due to the slow absorption of the local anaesthetic into the subarachnoid space. However, it has differences, causing less motor paralysis and being free from the more serious sequelae of subarachnoid injection. Headache does not occur. Chemical damage to the spinal cord and its roots is obviated. Infection, though it should not occur if a meticulous technique is performed, would not have such a disastrous effect as an infected spinal injection.

DIFFICULTIES OF EPIDURAL BLOCKS

Why, then, should epidural analgesia have been so infrequently used in the

past? The main drawbacks of the method are difficulty in locating the epidural space and the length of time necessary for the production of adequate analgesia.

Providing the anaesthetist is well practised in spinal puncture, lumbar epidural tap is considerably easier than it appears. Attention to detail and the exclusive use of one method are important if failures are to be avoided. Bromage (1954) reports fourteen failures in a thousand cases, but one should expect a 5 per cent failure rate. Failures are almost always due to subarachnoid tap.

Caudal analgesia on the other hand requires considerable skill and experience for consistent success. Failure rates of up to 20 per cent are reported in many series. These high rates are due not only to difficulty in inserting the needle correctly, but also to the failure of the injected drug to act satisfactorily even though it be in the sacral canal.

The time necessary to allow the local anaesthetic to produce adequate analgesia varies with the drug used, but can be a considerable drawback in coping with a long operating list. Procaine, cinchocaine and amethocaine require twenty to thirty minutes to produce their effect. The advent of lignocaine brought a considerable improvement, as it requires only six to twelve minutes for a lumbar epidural block and a little longer for a caudal block.

AIM OF THE PRESENT INVESTIGATION

If this time interval could be further reduced, so that for speed this procedure was comparable with spinal analgesia, there would be little to stop even the single-handed anaesthetist from performing several epidural cases in one list.

Hyaluronidase suggested itself as a likely agent to aid this speeding-up process. It was also thought that the enzyme might also increase the amount of spread of anaesthetic solution enabling smaller quantities to be used. This hope was not fulfilled, probably because fluid spreads very easily in the epidural space and any additional action of hyaluronidase is negligible.

The investigation, therefore, was concerned only with the speed of action of the injected local anaesthetic.

Properties of hyaluronidase.

Hyaluronidase is available as a white vacuum-dried powder, is very soluble in water but is destroyed by heat. It acts by liquefying the interstitial barrier which is normally gelatinous. To achieve this, hyaluronic acid, which gives the interstitial barrier its gelatinous character, is depolymerized (Britton and Habif, 1953).

The dosage is relatively unimportant as above an optimum dose there is no increase in effect, whilst in quantities many times in excess of the optimum it is nontoxic.

It has been used in local anaesthesia both to increase the spread of the anaesthetic and to speed up the onset of analgesia. However, hyaluronidase does not cause spread across fascial planes and its use does not lessen the need for accurate placement of the injection. In the epidural space it should not cause absorption through the dura mater, but it should penetrate the epineurium of the spinal nerves, and allow deep penetration within the nerve bundles.

When used with a local anaesthetic,

adrenaline (1: 100,000) must be added to prevent too rapid absorption, otherwise the duration of analgesia is too brief and there is danger of toxic reactions. When adrenaline is added, the duration is only slightly less than when no hyaluronidase is used.

METHOD OF INVESTIGATION

A series of patients undergoing gynaecological operations was studied. As far as possible, a standard technique was used in each case, the only difference being that half the cases received lignocaine and adrenaline, and half received lignocaine, adrenaline and hyaluronidase.

Premedication consisted of sodium amylobarbitone 3 grains (200 mg) in the early morning followed by papaveretum $\frac{1}{3}$ grain (20 mg) and atropine $\frac{1}{100}$ grain (0.65 mg) one hour before operation.

Caudal analgesia.

The patient was placed in the prone position with or without a small pillow under the pelvis. The skin was prepared with iodine and a small weal raised over the sacral hiatus. A spinal needle was inserted through the hiatus and advanced 1–2 inches up the sacral canal. If no cerebrospinal fluid appeared, a test dose of 5 ml of the anaesthetic mixture was given. If after five minutes no spinal analgesia was apparent, the rest of the calculated dose was injected. The dose depended on the operation, the size and age of the patient, but generally speaking, a total of 25 ml was used for pelvic floor repairs and 35 ml for lower abdominal operations. A 1.25 per cent solution of lignocaine was used. Adrenaline to make a 1 in 100,000 strength was added together with 1,000 Benger units of hyaluronidase in alternate cases.

Following injection, the patient was turned on to her back and tested for analgesia every $2\frac{1}{2}$ minutes until either the analgesia was adequate for the operation, or the maximum effect had been produced. Motor power of the lower limbs and abdomen was also tested.

Lumbar epidural analgesia.

The patient was placed on her left side in the usual spinal position. Through a skin weal, a short bevelled blunt spinal needle was advanced into the selected interspinous space, until it was well embedded in the interspinous ligaments, but superficial to the ligamentum flavum. A full 20-ml syringe was attached to the needle and a constant pressure exerted on the plunger whilst the needle was slowly advanced. As the needle pierced the ligamentum flavum and entered the epidural space, there was a sudden loss of resistance and the plunger moved forward easily. The syringe was disconnected and, if no cerebrospinal fluid appeared, a 5-ml test dose was given as before. After five minutes, in the absence of spinal analgesia, the main dose was given. For the average case, 25–30 ml were used. The patient was then turned on her back and tested for analgesia as with caudal blocks. The solution strengths were the same as in the caudal cases.

General anaesthesia.

After completing tests for analgesia, the patient was given 300–500 mg of thiopentone and unconsciousness was maintained with a mixture of nitrous oxide and oxygen (5: 2 litres per minute). Any deficiency in

the analgesia would soon become apparent and would require additional doses of thiopentone or small doses of relaxant. These additions were seldom necessary where pre-operative testing showed adequate analgesia.

RESULTS

Caudal blocks.

Forty-one cases were included in the series. There were eight apparent failures, not including cases where the needle could not be inserted into the sacral canal. Of the remaining thirty-three, seventeen received hyaluronidase and sixteen did not. Of those not receiving it, one case became entirely unco-operative and though adequate analgesia was present, one could not determine the time of onset. The speeds of onset are shown in table I.

TABLE I

Without hyaluronidase		With hyaluronidase	
Case No.	Speed of onset (min)	Case No.	Speed of onset (min)
1	10	1	5
2	10	2	12½
3	15	3	7½
4	12½	4	7½
5	10	5	5
6	10	6	7½
7	15	7	5
8	12½	8	5
9	10	9	10
10	10	10	5
11	7½	11	7½
12	15	12	10
13	10	13	5
14	10	14	10
15	12½	15	5
		16	5
		17	7½
Average	11.3 ± 2.29	Average	6.8 ± 2.39

The distribution of cases according to speed of onset is shown in figure 1, where the shift to the left of hyaluronidase cases is clearly seen.

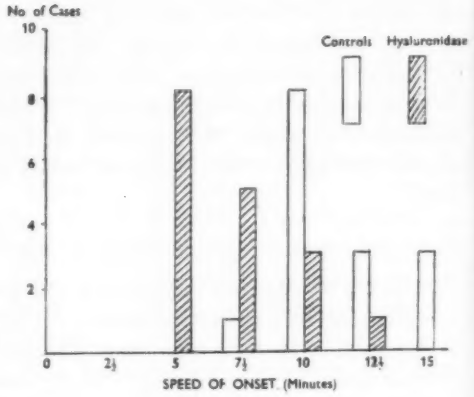

FIG. 1
Caudal blocks.

While the series is too small to draw definite conclusions, there was a considerably speedier onset in the hyaluronidase cases. Using hyaluronidase it was unusual for the onset to take longer than ten minutes, whilst without it, it was unusual to take under ten minutes.

Of the eight failures, four received hyaluronidase and four did not. In these, the patient would not admit to any pre-operative analgesia, but was generally managed quite well on the light general anaesthesia given to the other cases. The cause for this could not be determined, but possibly the analgesia was only partial. Unfortunately, there is no easily applicable objective test for analgesia.

Lumbar epidural block.

Sixty cases were given lumbar epidural blocks. Cases of spinal tap are not included. If this occurred the procedure was either abandoned or a low spinal was given. There were no failures comparable with those in the caudal series, i.e. where no analgesia resulted from an apparently

correctly placed injection. The analgesia was then more certain than with caudal block and the spread was more uniform and easy to control. Thirty cases received hyaluronidase and thirty did not. The speeds of onset are shown in table II.

TABLE II

Without hyaluronidase		With hyaluronidase	
Case No.	Speed of onset (min)	Case No.	Speed of onset (min)
1	10	1	7½
2	12½	2	5
3	7½	3	5
4	10	4	10
5	7½	5	7½
6	10	6	10
7	7½	7	7½
8	7½	8	7½
9	7½	9	10
10	10	10	7½
11	12½	11	7½
12	12½	12	7½
13	15	13	7½
14	7½	14	7½
15	10	15	7½
16	7½	16	7½
17	12½	17	5
18	10	18	7½
19	5	19	7½
20	7½	20	7½
21	12½	21	7½
22	10	22	7½
23	12½	23	7½
24	7½	24	7½
25	10	25	7½
26	7½	26	7½
27	7½	27	7½
28	7½	28	5
29	7½	29	5
30	7½	30	7½
Average	9.3 ± 2.36	Average	7.3 ± 1.39

Figure 2 shows the distribution and again there is a shift to the left indicating a speeding-up process.

It will be seen that the difference between the two groups is not so marked as with caudal block cases. However, there does appear to be trend in favour of the hyaluronidase group. If hyaluronidase is given it is possible to forecast with some accuracy that analgesia will be fully developed in 7½ minutes. Without hyaluronidase, while many cases will be ready in 7½ minutes, quite often one may have to wait appreciably longer.

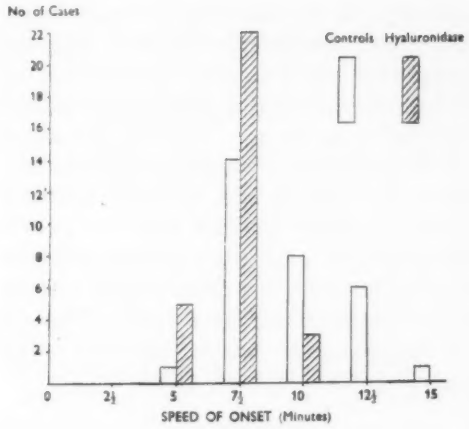

FIG. 2
Lumbar epidural blocks.

Toxic reactions.

Minor forms of reaction to the injected lignocaine were occasionally seen and all occurred in the caudal block cases. They consisted of tremors of the hands and facial muscles, and a feeling of dizziness and faintness. Such reactions, while not in themselves serious, may usher in a more serious episode with convulsions. Five cases presented such symptoms, three of whom did not receive hyaluronidase and two of whom did. There are several reasons why caudal block is more likely to produce toxic reactions than lumbar epidural blocks. Perforation of a blood vessel is more likely to occur. Secondly, in an attempt to reach a high enough level from the sacral hiatus,

considerable pressure may be used in injecting the anaesthetic solution. This results in too rapid an injection with consequent rapid absorption of local anaesthetic into the blood stream. Thirdly, the sacral canal is much more tightly packed with fat than the lumbar and thoracic epidural space. A fluid injected into the sacral canal will thus be under greater pressure than higher up in the epidural space where it can spread much more easily. The use of hyaluronidase had no apparent influence in producing these reactions.

DISCUSSION

From the investigations outlined above, it may be said that hyaluronidase speeds up the onset of epidural analgesia, this being more obvious in the caudal than in lumbar epidural analgesia. This difference between the two methods is probably linked with the differences in anatomy of the regions. During dissection of the sacral canal, one is struck by how tightly packed it is with fat and blood vessels, even in the emaciated bodies coming to the dissection room. In these circumstances, it is reasonable to suppose that the spreading effect of hyaluronidase may come into action in the sacral canal while in the lumbar and thoracic regions, the effect is less striking. This anatomical difference may also be a factor (among many others) why failures, or partial failures, occur in caudal blockade.

One interesting facet of the action of hyaluronidase in the epidural space concerns the actual mechanism of epidural analgesia. There are two differing theories on this mechanism. The first claims it to be a nerve block of the spinal nerves as they leave the dura mater in the intervertebral foraminae, while the second maintains that the anaesthetic agent is slowly absorbed through the dura and arachnoid mater to produce a subarachnoid block, the main body of the solution acting as a depot.

The present investigation appears to support the former theory. Moore (1953) states that fascia, fascial planes, periostium and fibrin walls act as barriers to the spread of solution containing hyaluronidase. It is therefore unlikely that hyaluronidase causes any local anaesthetic to be absorbed through the dura mater. Its effect must thus be extradural and assuming that hyaluronidase speeds the onset of analgesia, its most likely site of action is the spinal nerves themselves. It is tempting to think that the posterior root ganglia are directly affected. They are situated a considerable distance lateral to the main part of the dura (though the dura is prolonged out to reach each one). The lumbar and thoracic ganglia are opposite or within their respective intervertebral foraminae. In a small series of dissections of the sacral canal, it has been seen that the position of the sacral ganglia are variable, but most commonly, they are situated in a cluster round the termination of the dural sac at the level of the second sacral vertebra. To assume that the ganglia themselves are affected explains why sensory loss is much more marked than motor loss in epidural analgesia.

SUMMARY

A series of forty-one cases of caudal block and sixty cases of lumbar epidural analgesia are presented. In each group approximately half received hyaluronidase in the local anaesthetic solution, adrenal-

ine being added in each case. In the caudal group the cases receiving hyaluronidase had a speedier onset of analgesia than those not receiving it. In the lumbar epidural group, the same trend was seen though it was less marked. The possible mechanisms of this action and their bearing on the production of epidural analgesia are discussed.

ACKNOWLEDGMENT

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SOCIETY NEWS

GLASGOW AND WEST OF SCOTLAND SOCIETY OF ANAESTHETISTS

THE fourth meeting of the 1955–56 session was held on February 23, 1956, in the Royal Faculty of Physicians and Surgeons, 242 St. Vincent Street, Glasgow, C.2. Papers were read by Dr. Elizabeth Primrose, Western Infirmary, Glasgow; Dr. I. Levy, Stobhill General Hospital, Glasgow; Dr. W. Norris and Dr. P. Stuart, Royal Infirmary, Glasgow.

Dr. Primrose spoke on "General Anaesthesia in Obstetrics."

She first dealt with anaesthesia for the many minor elective procedures in obstetrics. As many were outpatients, atropine as premedication, followed by nitrous oxide - oxygen - Trilene, gave satisfactory conditions with rapid recovery. For external version the above sequence, with the addition of Scoline, was sufficient.

Dr. Primrose then reviewed the physiology of the foetal respiratory centre. The foetal respiratory centre was depressed by oxygen lack, acapnia and anaesthesia in the mother. All anaesthetic agents, volatile and nonvolatile, cross the placental barrier and depress the foetal respiratory centre. Cyclopropane/oxygen in a 30/70 percentage produces surgical anaesthesia without foetal depression. Morphine causes considerable foetal depression without sedative effect on the mother.

For emergency operations the anaesthetic requirements were (1) safety, (2) full oxygenation, (3) minimal foetal depression, (4) production of good operating conditions, (5) nontoxicity and noninterference with uterine retraction. These conditions could be fulfilled by a thiopentone, nitrous-oxide/oxygen, gallamine sequence. The importance of pre-operative gastric suction and intubation with a cuffed tube was emphasized. Thiopentone was contra-indicated when delay in extraction of the infant was likely. For other emergencies, nitrous-oxide, oxygen and ether was satisfactory.

Dr. Levy spoke on "Diaphragmatic Susceptibility to Flaxedil."

Different muscles varied in their susceptibility to the competitive relaxants, curare and Flaxedil, and always relaxed in the same definite order—ptosis, extra-ocular muscles, larynx, limbs, abdominal, intercostal and diaphragm last. Muscles of a certain structure are more easily relaxed, the reason for this being unknown. There are two types of skeletal muscle: (1) red, (2) white. The red is more primitive, has abundant sarcoplasm, a high concentration of myohaemoglobin and a low metabolic rate. The white has little

sarcoplasm, little myohaemoglobin and a high metabolic rate. Red muscle is affected last by curare and Flaxedil. The diaphragm is a red muscle.

Dr. Levy reviewed the work on flaxedil done in 1949 by Mushin and his colleagues. The injection intravenously in conscious persons of Flaxedil in a dose of approximately 1 mg/kilo body weight produced a complete paralysis of the flexors of forearm and recti abdomini without a decrease in pulmonary ventilation. Paton and Zaimis in 1950 showed that adrenaline decreases the effect of curare and Flaxedil and especially so on the diaphragm.

Dr. Levy had attempted to measure the effect of small doses of Flaxedil on the respiratory muscles during anaesthesia. By means of an attachment to the reservoir bag of the Boyle's machine traces were obtained of its movement during anaesthesia. Following the exhibition of small doses of Flaxedil (40 mg) the traces showed, after a lapse of approximately 30 seconds, a diminution of the tidal exchange which lasted between 1½ and 3 minutes. In three cases a rise in tidal exchange for about 10 seconds preceded the decrease in respiratory ventilation.

Dr. Levy came to the conclusion that one could obtain relaxation with small doses of Flaxedil, repeated if necessary, with adequate ventilation, except, perhaps, for a minute or two. He hoped in further experiments to estimate the changes, if any, in carbon dioxide tension during the period of depressed respiration.

Dr. Norris and Dr. Stuart spoke on "Cardiac Arrest During Trilene Anaesthesia."

A critical survey of the literature pertaining to cardiac arrest during Trilene anaesthesia was presented. Of twenty cases reviewed by Ostlere (1953) only in three was he prepared to incriminate Trilene. Drs. Norris and Stuart considered a further five of these twenty merited inclusion as Trilene induced cardiac arrest. Burnstein in 1954 reported one case of cardiac arrest during Trilene analgesia. Lock and Greiss reported three cases in obstetrics of cardiac arrest under Trilene.

Seven previously unpublished cases of cardiac arrest under Trilene collected from anaesthetists in the West of Scotland were presented and discussed. In four cases the arrest occurred before surgery was started. The similarity of the cardiac failure in these cases to that described by Snow when reporting primary cardiac arrest under chloroform anaesthesia was stressed.

Trilene, being a powerful analgesic neither irritant nor explosive, has enjoyed a considerable popularity in this country since its introduction. Trilene, however, bears a strong resemblance to chloroform, and although the risk of cardiac arrest may not be so great as with chloroform the speakers thought it was not so rare an occurrence as the literature would suggest. The place of Trilene in modern anaesthesia was very limited and in the absence of strong indications for its employment, other and safer agents should be used. When used the possibility of cardiac arrest should be borne in mind and this risk balanced against the advantages to be gained. There is still a place for a safe noninflammable volatile anaesthetic agent, should such be discovered.

FACULTY NEWS

RESEARCH DEPARTMENT

The Council has been pleased to approve the recommendation of the Board of Faculty that Dr. Ronald Woolmer (Reader in Anaesthetics, University of Bristol) be appointed Director in Charge of the Research Department of Anaesthetics in the Royal College of Surgeons.

SCIENTIFIC MEETING

There will be a Scientific Meeting held on Saturday, May 5, 1956, at 10.30 a.m. The speakers, on the Adrenal Gland, will be:

Professor J. H. Burn
Dr. E. S. Scowen
Dr. A. W. Spence
Professor W. W. Mushin

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